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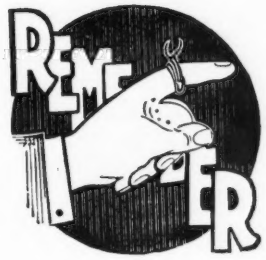

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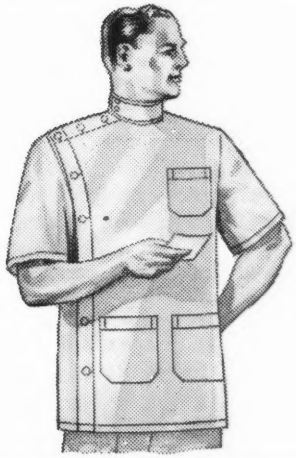

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COCCIDIOIDOMYCOSIS*

By JACK D. KIRSHBAUM, M.S., M.D., F.A.C.P.**

Coccidioidomycosis, known also as coccidioidal granuloma, is caused by the fungus Coccidioides Immitis and was first described by R. Wernicke[1] in 1892. The disease is endemic in the central portion of California, especially in the San Joaquin Valley, and was known for many years as valley fever. The disease is prevalent in dry and dusty areas and that explains the high incidence of the disease in the San Joaquin Valley. During the war over 6,000 cases were diagnosed in the army in troops stationed in California, Arizona and New Mexico. In view of the fact that these soldiers are now living in all parts of the United States, it is important that physicians become alerted to the possibility of the presence of coccidioidomycosis in their patients.

The infection is acquired by inhaling the spores of C. Immitis, known as the chlamydospores and arthrospores. Within the human body the spores mature into spherules. The spherules develop endospores and upon rupturing of the capsule the endospores escape into the tissues. The spherules are easily identified in the tissues. They have a double-contoured, highly refractile capsule and are filled with spores. The spherules vary in size from 2 to 80 microns. The mycelia seen in culture is never found in the tissues. Cases have been known where the infection was acquired through abrasions or lacerations in the skin. It usually requires from one to three weeks incubation period before symptoms become manifested. Many patients acquiring the infection may not manifest any active clinical symptoms at all but will show a positive skin reaction to the coccidioidin filtrate. About 40% of the males will develop respiratory symptoms, whereas females will show an increased frequency of erythema nodosum. The latter results in a somewhat higher proportion of clinically manifested cases of the disease. It is now known that erythema nodosum is an allergic manifestation and is a complication of the initial respiratory infection.

Coccidioidal granuloma or so-called disseminated coccidioides was the only form recognized until Gifford[2] in 1935 reported that Coccidioides and "San Joaquin Valley Fever" were the same infection. Gifford recovered the organisms from the sputum of a patient who presented the skin manifestations of erythema nodosum and had so-called "Valley Fever". Thus the relationship of the two diseases was established.

The disease has been transmitted experimentally from human to animals but has never been seen transmitted from human to human. Rosenthal[3] believes the disease is contagious. This has not been confirmed by other workers, and both Smith[4] and Gifford deny the possibility. Although the morbidity is high in Kern County, California, the mortality is low. The disease is usually ushered in with mild upper respiratory symptoms and very often the diagnosis is not suspected. Patients with erythema nodosum as a rule never develop the fatal disseminated form. These patients usually come into the hospital complaining of bumps in the skin. The lesion is not painful. The sites usually affected are the extremities and the skin over the chest. The abdomen is usually spared.

Clinically coccidioidomycosis may be classified into the following types:

A. Primary or Pulmonary form.
B. Secondary or Cutaneous form.
   Acute—Erythema nodosum or Erythema multi-forme
   Chronic—Granuloma-isolated to an organ i.e. bone, lung, skin, etc. (non-fatal).
C. Fatal Form (so-called disseminated coccidioidomycosis)

The primary or pulmonary form presents a clinical picture of an acute upper respiratory infection, characterized by cough, chest pain and fever. Chills may or may not be present. X-ray examination of the chest is usually suggestive whereas skin tests and serological findings are fairly reliable and diagnostic. The cutaneous manifestations represents an allergic response and the histological picture is not specific.

In the granulomatous form, the biopsy of the lesion reveals typical spherules of C. Immitis.

*Lecture delivered at The Chicago Medical School Seminar October 6, 1948.

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**Former Associate Professor and Acting Head of the Department of Pathology—Chicago Medical School.

This type may be present for many years. The skin test is usually positive.

The disseminated or fatal form often comes on after several weeks or months following the primary infection.

Of great diagnostic aid is the skin test. The material used in our laboratory is supplied by Dr. Charles E. Smith of Stanford University. It is a filtrate of liquid cultures of coccidioides immitis. We use a dilution of 1 to 100, and it is found to be of sufficient strength. Higher dilutions are apt to produce false reactions. However, in some of our cases of the disseminated form we have noticed a negative skin test using a dilution of 1 to 100, whereas by increasing the strength to 1 to 10 the reaction has been positive. From June 1947 until July 1948, we skin tested 864 patients at the Kern General Hospital, of which 156 were positive or 18 per cent. During this same period 2753 patients were skin tested from the clinics, of which 563 were positive or 20 percent. A total of 3617 skin tests yielded 719 positive cases or 19 per cent. These patients were also tested with tuberculin. The latter does not interfere with the coccidioidin skin test.

Another important diagnostic procedure is the serological test for coccidioidin infection. These tests were performed in the laboratory of Dr. Charles E. Smith of Stanford University and have proven to be of diagnostic and prognostic value. In this test one examines for precipitins and complement fixation. The precipitins appear before the complement fixation becomes strongly positive. Table 1 illustrates a group of fatal and non-fatal patients whose serum was examined for precipitins and agglutinins. The prognosis and diagnosis was usually interpreted correctly by Dr. C. Smith. The spinal fluid usually shows the same changes found in the serum in cases of coccidioidal meningitis. In the fatal cases the first (PM 149) was a 34 year old white male who had symptoms of meningitis for 3 years. His

SEROLOGICAL TESTS FOR COCCIDIOIDAL INFECTION

	COMPLEMENT FIXATION TEST								PRECIPITIN TEST					
	1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256	Undiluted	1:10	1:40	1:100	PROGNOSIS	DIAGNOSIS
D. R.	±	±	0	0					++++	++++	++++	0	Good	Primary Active Infection
H. W.	++++	++++	++++	++++	++++	++++	++++	±	0	0	0		Hopeful	Primary Infection
D. F.	++++	++++	±	0					+++	+++	0		Hopeful	Active Primary Infection
R. W.	++	±	±	0					++++	++++	++++	0	Hopeful	Active Primary Infection
L. M.	++++	±	0	0					++++	++++	++++		Hopeful	Active Primary Infection
D. W.	++++	++	0	0					0	0	0		Good	Active Primary Infection
C. F.	++++	++++	++++	++++	++++	++++	++	0	++++	++++	+++	0	Grave	Abscess with Dissemination
	FATAL CASES													
PM 149	++++	++++	++++	++	0				0	0	0		Grave	Meningitis
PM 114	++++	++++	++++	++	++++	0			0	0			Grave	Meningitis
PM 222	++++	++++	++++	+++	0				++++	++++	+++	0	Grave	Primary Disseminated
PM 199	++++	++++	++++	++++	++++	0	0		++++	++++	++		Grave	Primary Disseminated

serum on repeated examinations indicated a chronic infection. In cases PM 222 and PM 199 the sera suggested a severe primary dissemination. In case D.R. we have an example of a young resident who recently contracted his primary pulmonary infection while working at the hospital. His complement fixation test was weakly positive up to 1 to 4 dilution, while his precipitin tests were strongly positive. Such a case must be watched very closely. Serological tests will be repeated at regular intervals. It is six months since he contracted coccidioidomycosis and at present he appears to be handling his infection favorably as indicated by serological and X-ray examinations.

We have recently reviewed 45 fatal cases of disseminated coccidioidomycosis coming to autopsy from a series of 2890 consecutive necropsies, an incidence of 1.5 per cent. Our series constitutes the largest number of fatal cases to be reported from one institution. In 1936 the Los Angeles General Hospital files contained 36 fatal cases of coccidioidomycosis which were studied from a series of 12,000 autopsies. In 1946 Forbus[5] reported 50 cases taken from the files of the army Institute of Pathology. These cases were collected from all parts of the world in the armed forces. As to race there were colored—19 cases or 42.4%, white—12 cases or 26.6%, Filippino—11 cases or 24.4%, Mexican—2 cases or 4.4% and Indian—1 case or 2.2%. The high incidence in the colored race is probably due to the same social and economic causes similarly found in tuberculosis. The youngest patient in our series was 5 months and the oldest was 64 years. They were distributed as follows: up to 1 year 1 case; 1 to 10 years 4 cases; 11 to 20 years 2 cases; 21 to 30 years 14 cases; 31 to 40 years 18 cases; 41 to 50 years 5 cases, and over 60 years 1 case. Between 51 and 60 years there were no cases seen.

Anatomically no organ is immune in coccidioidomysosis. The lungs showed the highest incidence, 37 cases. The brain was involved in 23 cases in the form of a basillar meningitis. The other organs affected in their order of frequency were lymph nodes, spleen, bones (vertebra particularly), skin, liver, prostate, kidney, heart, and adrenal. The gross examination of the organs is often confused for tuberculosis. Cavitation in the lung may mimic tuberculosis, however in coccidioides the wall is often much thinner. The caseous form of pulmonary coccidioidomycosis may also be mistaken for tuberculosis. In these cases histological sections reveal an inflammatory exudate, large numbers of spherules with endo-

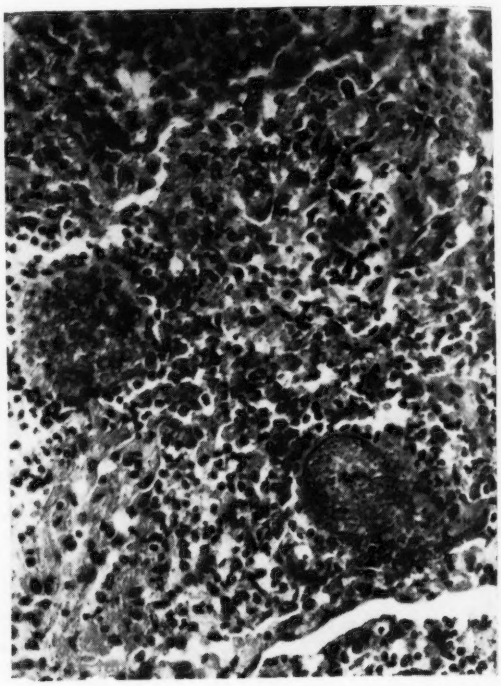

FIGURE 1. Section of lung showing pneumonic process. Note single spherules of C. Immitis. H.E. x 100.

spores (see figure 1) and ruptured spherules with escaping endospores (see figure2). Typical tubercle formation is not common as seen in the chronic granuloma form. In the latter, epithelioid cell tubercles with giant cells are common. The giant cells often show engulfed spherules (see figure 3). A nodular form is occasionally seen simulating a neoplasm. Some cases of coccidioidal osteomyelitis of the vertebra produce either an unilateral or bilateral psoas abscess which grossly cannot be differentiated from tuberculosis. In several of our cases the diagnosis was not suspected clinically. Spherules usually can be demonstrated in smears made from the purulent exudate stained with hematoxylin and eosin. The sternum and the skull are also frequent sites involved.

In coccidioidal meningitis the exudate is found usually at the base. The exudate becomes thick and firm and causes an obstruction of the circulating spinal fluid. This results in a marked in-

ternal hydrocephalus and final death of the patient.

The skin when affected may be the site of sinus

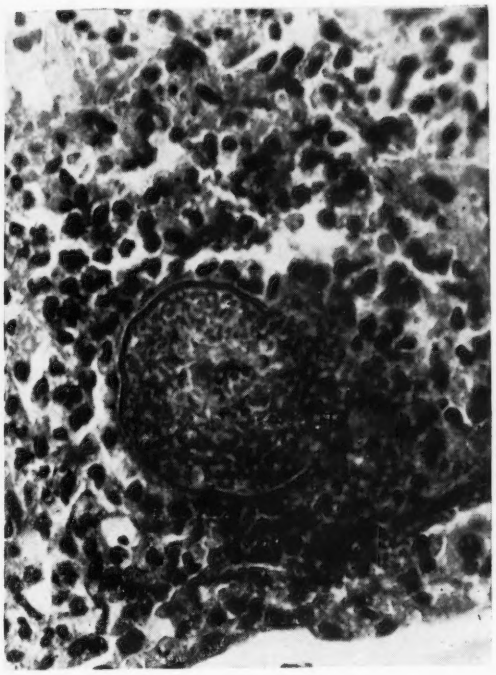

FIGURE 2. Spherule showing rupture of capsule and escape of endospores. H.E. x 200.

formation of a chronic nature. The disseminated form of coccidioidomycosis may be associated with a pustular eruption in the skin. In one of our cases the face was severely affected. Smears from one of the pustules showed large numbers of spherules.

Symptoms:

The primary infection in the lung is usually characterized by a cough, malaise, chest pain, anorexia and a slight fever. After two to four weeks the symptoms usually subside. In the progressive type the patient may also have high fever, chills, and night sweats. If the meninges become involved the patient develops headaches, nausea and vomiting. These patients with meningitis differ from tuberculous patients in that they are not in a continuous stupor but are rather quite alert when they are free from their headaches and vomiting. Some of these patients may be up and about for weeks or months at a time. In the meningeal form the spinal fluid examination is very important as indicated by the agglutination tests and the colloidal gold. The curve takes on a paretic appearance. The cell count is increased while the type cell is not characteristic. Some cases show a lymphocytosis and in others the polymorphs are increased. The sedimentation rate is usually increased.

X-ray examination of the chest or bones is not specific. In the chest the changes may simulate tuberculosis or pneumonia. The bones show an osteolytic process similar to tuberculosis. A biopsy of the bone lesion usually reveals the spherules, and the correct diagnosis is thus made. Large hilar lymph nodes on X-ray films have been mistaken for Hodgkin's Disease. In several cases sternal puncture permitted the recovery of spherules and a diagnosis of coccidioidal granuloma in the sternum prior to X-ray examination was made.

Summary and Conclusion

Although coccidioidomycosis is extremely rare in the middle west, it behooves the clinician to be alerted to the possibility of this infection, especially if one has been a member of the armed forces during the war and particularly if the patient was stationed in the southern part of California, Arizona, New Mexico, or western Texas. These patients should have skin tests with coccidioidin (dilution of 1 to 100), X-ray

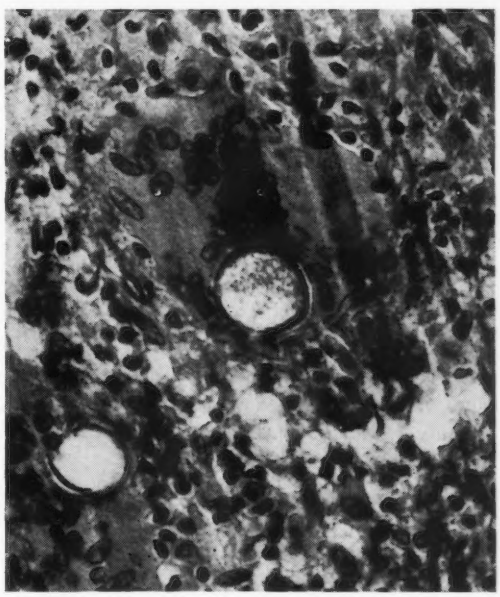

FIGURE 3. Section shows granulomatous reaction with giant cells containing degenerative forms of C. Immitis. H.E. x 590.

examination of the chest and sputum examination for spherules.

In suspicious cases of meningitis the complement fixation and precipitin tests should be made on the sera and spinal fluid. The colloidal gold gives a paretic type of curve.

In active cases the sedimentation rate is increased. The blood may reveal an eosinophilia up to 15 per cent. Any suspicious lesion should be biopsied for the presence of spherules. Aspirated material or sputum should be cultured using Sabouraud's media, and may be inoculated into guinea pigs.

Although the morbidity has been high for coccidioidomycosis in the "San Joaquin Valley," the mortality has been low and is exceeded by tuberculosis.

Since 1933 there has been 45 cases coming to autopsy. As to race there were 42% Negroes and 24% Filippinos. The males are more frequently affected than females, a ratio of 3 to 1. The majority of the patients were between 21 to 40 years of age.

Coccidioidomycosis is a granulomatous infectious disease. The granulomatous form resembles tuberculosis and the acute suppurative form resembles the ordinary pyogenic disease.

The most frequent sites of the lesions which resulted from the dissemination of C. Immitis were the lungs, brain, lymph nodes, bones, and skin. The above indicates a hematogenous route, as well as local lymphogenous from the lungs to the regional lymph nodes.

The characteristic reaction of the body to C. Immitis is inflammatory and may be either suppurative or granulomatous.

REFERENCES

1. Wernicke, R.: *Uber einen Protozoenbefund bei mycosis fungoides,* Zentralbl. f. Bakt. 1892, 12:859.

2. Gifford, M. A.: *Annual Report Kern County Health Department for the Fiscal year July 1, 1935 to June 30, 1936,* pp. 22-23.

3. Rosenthal, S. R., and Routien, J. B.: *Contagiousness of Coccidioidomycosis.* An experimental study, Arch. Int. Med., 1947 Lxxx, 343-357.

4. Smith, C. E. *Coccidioidomycosis,* Med. Clin. North Am. 1943, XXVII, 790-807.

5. Forbus, W. D. and Bestebreurtje, A. M. *Coccidioidomycosis: The Military Surgeon Vol. 99,* Nov. 1946, No. 5 653-719.

RESPIRATORY AND METABOLIC DISTURBANCES AND THEIR LABORATORY DIFFERENTIATION

By WALLACE L. SALZMAN, M.B.

IN HOPE of bringing to light some of the concepts of electrolytic equilibrium which might be of clinical value, we are presenting information obtained from the works of H. L. Gamble and those other men who have delved into the study of extracellular fluid and its relation to pathophysiology.

Extracellular fluid, replaces in its essential features, and still closely resembles, the external environment of the early forms of sea life. This fact may act as a reminder of the close relationship existing between cells of all types, be they by themselves, as the protozoans, or living in groups with differentiated functional activities as the metazoans. The aqueous medium surrounding the tissue cells is the vehicle for waste and nutrient transport and its constantcy in osmotic pressure, ionic concentration, pH and temperature, measures the normal physico-chemical activity within the body. When these qualities of extracellular fluid are normal, we may assume that normal tissue metabolism is taking place, and with a change in the components of the fluid a similar change can be expected within the cell itself. We can therefore see that extracellular fluid not only maintains the cell, but also reflects cellular disability.

Although constancy of these vital factors is essential for the maintenance of life, a yielding system is the only one which could come with a unit like the human body, whose water intake is unpredictable and whose output and intake vary with the weather, the activity and the time of day. By constancy we do not mean that there is one level of normal, but rather that there exists a normal range, which when not maintained is reflected by the body in the symptomatology of some pathological entity.

There are many mechanisms which the body may utilize to maintain the pH at a normal level of approximately 7.4. Except for carbonic acid, the bicarbonate ion and the proteins, the level of the plasma components is controlled by the kidney. The range of the hydrogen (or hydronium) ion concentration compatible with life is from one ten millionth to one one hundred millionth of a gram per liter. The basis of control of ionized hydrogen at this ultriminute concentration which the biologic processes require is the almost uniquely small extent of hydrogen dissociation from the largest end product of metabolism, carbonic acid. The level of carbonic acid is controlled by the respiratory mechanism and in the presence of its salts, the slight extent of dissociation of hydrogen becomes even smaller, due to the common ion effect:

$$HHCO_3 \rightleftarrows H^+ + HCO^-_3$$
$$BHCO_3 \rightleftarrows B^+ + HCO^-_3$$

This gives the blood an excellent buffering system. The best buffering range of carbonic acid and its salts is at a pH of 6.1, but with the aid of the respiratory control of the carbon dioxide concentration in the alveoli, and by this means in the blood stream, the use of this method is made feasible.

At a pH of 7.4 there are 3 vol % of carbonic acid in the blood and 60 vol % of HCO_3 that the ratio between the two compounds is 1/20. This ratio should be remembered, because no matter what the total CO_2 combining power might be, as long as the ratio between the carbonic acid and bicarbonate maintains itself at this normal physiologic level, the pH of the blood will remain normal, but with a change in either direction there will be a change in the pH.

Study of the pathogenesis of metabolic and respiratory acidosis and alkalosis reveals several basic principles which if understood will clear up all the confusion related to this subject. *In metabolism disturbances there is primarily a change in the bicarbonate ion and in respiratory disturbances the primary change is in the carbonic acid level of the blood.*

Disturbances of a metabolic nature may be divided into 3 main headings:

1. Impairment of Renal Function.
2. Loss of Gastrointestinal Secretions.
3. Abnormal Acids in Extracellular Fluid.

1. Impairment of Renal Function

As stated previously, the kidney controls the level of all plasma constituents, except the carbonic acid, bicarbonate and the proteins. If, as in chronic nephritis and other conditions manifested by poor kidney function there is a retention of normally excreted substances as sulfates, chlorides and phosphates, there must be an associated decrease in another anion, so that there is the same number of milliequivalents of both anions and cations. The most labile plasma component not under the control of the kidney is the bicarbonate ion and it changes inversely to the change of the retained waste products. With a decrease in the bicarbonate ion, we note a change in the 1/20 ratio, and unless a corresponding decrease in the carbonic acid takes place the pH of the blood will be changed. By respiratory acceleration the body attempts to compensate in the following manner. The blowing off of CO_2 decreases the CO_2 partial pressure in alveoli to less than normal. This decrease is followed by a decrease in the carbonic acid of the blood, which depends on alveolar concentration for the maintenance of its normal physiologic level. If the retention is severe and the level of retained wastes mount rapidly, the hyperpnea is unable to completely compensate for the fall in the bicarbonates. The ratio between the bicarbonates and carbonic acid is permanently changed, and this results in a permanent change of the pH. Although there is a marked drop in the total CO_2 combining power, there is a relative greater amount of carbonic acid which results in an acidosis. The acidosis is the result of a primary change in the bicarbonate fraction and is therefore known as a metabolic acidosis.

In Nephrosis there is a marked albuminuria which lowers the plasma protein to pathologic levels. If this were the only change we would have a need for a greater amount of anions, and the bicarbonates would be raised. The drop in the protein, however, is accompanied by a marked rise in the blood chlorides which more than compensate for the protein loss. This hyperchloremia produces a decrease in the bicarbonate ion, just as the retained products of kidney failure did in the above example. It is because of this, that we frequently find nephrotics in slight acidosis. Whether or not the rise in chlorides is due to poor kidney function, or is a method that the body uses to compensate for protein loss and maintain electrolytic equilibrium, is not yet known. If there is a marked loss of fixed base such as the

sodium ion, the decrease in cations will be immediately followed by a decrease in anions and once again the level of bicarbonate may be changed. This is the situation which we may find in adrenal disorders such as in Addisons disease.

2. Loss of Gastrointestinal Secretions

Depending upon the character of the fluid lost in diarrhea and regurgitation, we have a variance in the resulting status of the electrolytic balance. The electrolytic composition of the gastrointestinal secretions at various levels of the tract differ. Gastric juice has nearly all its anions in the form of chlorides; pancreatic juice has a high concentration of bicarbonates, although some chlorides are also present; hepatic duct bile has a greater amount of chlorides than bicarbonates, but the concentration of the fixed base sodium is rather high in this secretion, and a loss of sodium would be mirrored by an anion loss of bicarbonates; the jejunal secretions have a content similar to bile. Knowing the marked difference in electrolytic content makes one more readily understand why obstructions at different levels of the intestinal tract produce completely different clinical pictures. The contents of the regurgitated fluid will determine whether or not a patient will go into acidosis or alkalosis. In Hypertrophic Pyloric stenosis there is a great loss of chlorides. The rapid depression of the chlorides, must be compensated for by a rise in another anion so that there will be electrolytic balance. The rise in bicarbonate is at first easily compensated for by a depression of respiration. The shallow breathing causes a rise in the CO_2 partial pressure of the alveoli and a corresponding rise of the carbonic acid level in the blood. If the hypochloremia produced by constant regurgitation is very marked, the body is unable to produce a rise in the carbonic acid which will be sufficient to maintain a 1/20 ratio. It is when this crisis has been reached that we have a relatively greater amount of bicarbonate in the blood and a resulting metabolic alkalosis. Note that the primary change was once again of the bicarbonate ion, and for this reason we label the alkalosis in the metabolic classification.

If the obstruction is further down and the vomitus contains a high percentage of bicarbonate and fixed base the resultant situation is a metabolic acidosis. One may logically determine what the result of the electrolytic loss will be. If the bicarbonates are primarily decreased we have a terminal acidosis, if they are increased we have a resultant alkalosis.

The marked loss of fluids and dehydration; the lack of glucose and starvation all play a role in the final picture of gastrointestinal emissions. The dehydration results in poor kidney function and a retention of waste phosphates, chlorides and sulfates. The starvation produces an increase in the concentration of ketone bodies in the serum. When both of these factors are taken into consideration the terminal picture may be somewhat different and apparently paradoxical. If the obstruction is located high in the duodenum, one must expect an alkalosis due to the marked chloride loss and the bicarbonate increase. If, however, the patient is in a cachectic state and is starving, there will be an increase in the concentration of ketones in the blood serum which will force the bicarbonate level down and produce an acidosis rather than an alkalosis.

3. Abnormal Acids in Extracellular Fluid.

We find in diabetes a liver controlling a sugar level which has been markedly raised because of pancreatic deficiency or pituitary and adrenal excess. If there is sufficient glycogen in the liver to produce glucose, or if the level of glucose in the blood is high enough to maintain the new high pathological level, there will be no attempt on the part of the liver to utilize its fat and protein deposits. If, however, according to Soskin, the glucose level is not maintained, the liver will begin metabolizing an excess of ketone bodies which the muscles of the body will be unable to utilize. This rise in ketone bodies produces a depression of bicarbonate and results in a metabolic acidosis. It is this acidosis which may be most severe because of the rapid formation of ketone bodies. The typical Kussmaul breathing is the attempt on the part of the body by deep inspiration to bring the carbonic acid level of the blood down as rapidly as the bicarbonates fall. However, as may be noted by the large number of patients brought into the emergency room in severe acidosis, the mechanism of compensation is usually unsuccessful.

We have briefly discussed the various pathogenesis of metabolic acidosis and alkalosis, due to primary bicarbonate change. We must now recognize the existence of a respiratory type of both types of pH change, which may be difficult to differentiate from the metabolic clinical pic-

ture. In the respiratory disturbances the primary change is in the carbonic acid level. There is an attempt on the part of the body to bring about a similar change in the bicarbonate as will soon be described.

By means of hyperventilation we may primarily produce a decrease in the partial carbon dioxide pressure in the pulmonary alveoli. This, in turn, will produce a decrease in the serum carbonic acid. With a lowering of the carbonic acid level the 1/20 ratio is disturbed and the bicarbonate is eliminated in order to maintain a physiological pH. It is due to the body's inability to completely compensate for the primary change that we find a relative greater amount of bicarbonate in the serum, which produces an alkalosis. This is a respiratory alkalosis because the primary disturbance was one of respiratory abnormality. Hyperventilation may be due to over-anxiety as in the hypervnetilation syndrome, to salicylate intoxication, or it may manifest itself as part of a postencephalitic syndrome. The Hyperpnea may appear similar to that which we find in metabolic acidosis, but in respiratory alkalosis it is primary while in metabolic acidosis it is secondary. It was thought at one time that the salicylates produced an acidosis and resulted in the hyperpnea, but this was found not to be true. The salicylates apparently act on the central respiratory control centers directly.

The normal CO_2 partial pressure in the alveoli of the lung is 6 vol %. Since the coefficient of absorption into the serum is 50%, the amount of CO_2 in the form of carbonic acid found in the serum is 3 vol %. If there should be an enlargement of the alveoli with a relative loss of elasticity of the pulmonary parenchyma, there would be a stagnation of air in the alveoli and the CO_2 partial pressure would rise considerably. This is the process which is taking place in Emphysema. The rise in alveolar partial pressure produces a rise in the carbonic acid level of the serum. Once more we find an attempt at compensation by raising bicarbonates in order to maintain the 1/20 ratio, but as we have found in previous conditions the compensation is incomplete with a resulting respiratory acidosis.

In reviewing the above we note the following:

1) In metabolic acidosis there is a decrease in the total CO_2 combining power.

2) In respiratory alkalosis there is also a decrease in the total CO_2 combining power.

3) In metabolic alkalosis there is an increase in the total CO_2 combining power.

4) In respiratory acidosis there is also an increase in the total CO_2 combining power.

How may we differentiate between the first two and the second two if the CO_2 change is in the same direction. Clinically, the individual who is in respiratory alkalosis may show signs of tetany due to a decrease in the level of ionized calcium in the serum. This is due to increase of non-diffusable calcium with greater alkalosis. If, however, we have cerebral edema accompanying a metabolic acidosis the signs of depression and stupor may have an excitatory phase superimposed. If we are familiar with the history of the patient, no problem is posed and we may treat accordingly, but we certainly should not treat a patient for an acidosis when he is in alkalosis. The problem may be easily solved by determining the pH of the blood, for in alkalosis the pH will be above normal and in acidosis the pH will be below normal. We can readily see that if the pH of blood is determined at the same time that the CO_2 combining power is determined, a clearer picture of the process which is going on will be obtained.

New Books in the Library

Advances in military medicine. 2 vols. 1948.
Alexander & French. Psychosomatic medicine. c1948.
A.M.A. Interns' manual. 1948.
A.R.N.M.D. Frontal lobes. 1948.
Beach, F. A. Hormones and behavior. c1948.
Bloom, W., ed. Histopathology of irriation. 1948.
Cunningham, C. H. Laboratory guide in virology. c1948.
Donner Foundation. Index to literature of experimental cancer, 1900-35. c1948.
Hoffman & Davis. Write and speak better. c1937.
Pincus & Thimann. The hormones. Vol. 1. c1948. (In 2 vols.)
Ponder, E. Hemolysis and related phenomena. 1948.
Shattuck, L. Sanitary commission of Massachusetts, 1850. 1948.
Stitt, Clough & Barnham. Bacteriology, haematology and parasitology. 10th ed. c1948.

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SPECTROPHOTOMETRIC DETERMINATION OF EPINEPHRINE AND OF AN EPINEPHRINE-LIKE SUBSTANCE WHICH CAN BE OBTAINED FROM AUTOLYZING ADRENAL GLANDS

By RICHARD G. ROBERTS, Ph.D., and DORIS M. HILKER

From the Department of Biochemistry of The Chicago Medical School

IN AN investigation of the dialysis of various autolyzing glands it has been found that an epinephrine-like substance can be obtained from whole adrenal glands by mincing the glands in a food chopper, grinding the product with sand in a mortar and then dialyzing the paste against distilled water at 10° C. The pressor substance found in the dialysate has been named "epinephrine like" since the pressor curve given by it when it was injected into dogs was practically identical with the pressor curve given by the P.D. adrenalin control, but the pressor substance could not be precipitated from solution by the addition of strong ammonium hydroxide as can be done with free adrenalin base. The dialysate which contained the pressor substance was colored a bluish-violet which resembled strongly the color given by a biuret reaction. The bluish-violet color continued to dialyze from the bag for ten days after which the dialysate became yellowish. The pressor substance continued to dialyze from the bag for seventy days. The dialysate never turned pink when left exposed to air as a solution of adrenalin will do, although the emerald green Vulpian reaction with ferric chloride could be obtained at any time. An appraisal of these results would indicate that the dialysate was an epinephrine conjugate. Later work showed that the conjugate yielded epinephrine on acid hydrolysis.

The origin and chemical nature of the bluish-violet color, however, remained unexplained. Therefore, dialysates were prepared from pituitary, thyroid, kidney, pancreas, spleen and heart tissue, but the bluish-violet color did not develop. Also, several hundred grams of adrenal tissue were carefully ashed in a muffle furnace at 600° C and varied quantities of gray ash were added to P.D. adrenalin in aqueous solution at pH values ranging from pH 1.0 to pH 7.0 but no color developed, also when stainless steel knives were substituted for the food chopper no color developed in the dialysate. Guided by the results obtained, various metallic salts were added to solutions of P.D. adrenalin. One of the salts tried, ferric ammonium oxalate, gave a color which to the unaided eye, resembled the bluish-violet color of the dialysate from the adrenal glands. Spectrophotometric curves of both solutions were made on a Beckman quartz spectrophotometer and it can be seen (Fig. 1) that the two curves are almost identical. A dialyzing bag to which iron oxide had been added in addition to the ground adrenal glands gave a darker blue-violet colored dialysate than the bags to which no iron had been added. The dialysate was pink when sodium oxalate was added in the same way. An attempt was made to extract the bluish-violet color from solution by such solvents as ether, alcohol, chloroform, benzene and carbon tetrachloride, but this was unsuccessful. In comparing the bluish-violet dialysates with solutions of adrenalin to which

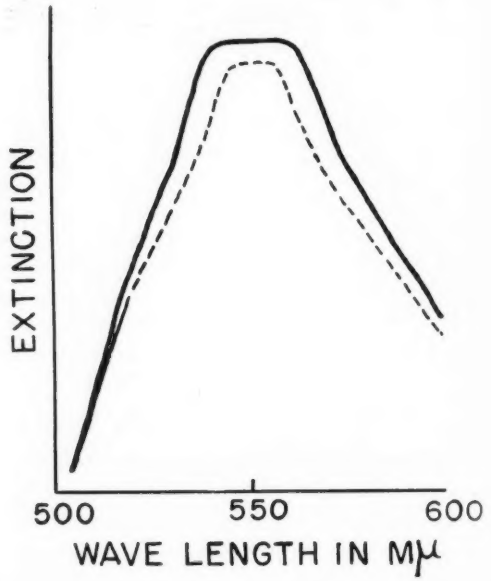

FIGURE 1. The broken line represents the extinction curve that was obtained by using P.D. adrenalin and ferric ammonium oxalate. The unbroken line represents the extinction curve obtained from autolyzing adrenal glands. The P.D. adrenalin curve is slightly sharper than the curve from the dialysate but both curves center at 552 mili micra. The depth of the absorbing liquid was 1.0 cm.

ammonium oxalate had been added, 10% HCl was added to both solutions; the dialysate turned colorless and the solution of adrenalin and ferric ammonium oxalate became a light yellow. When 10% NaOH was added to the dialysate it turned pink, but an orange precipitate formed when 10% NaOH was added to the adrenalin and ferric ammonium oxalate solution. These results led us to the conclusion that the bluish-violet color was a complex of adrenalin and ferric iron with some organic compound but not necessarily with an oxalate.

Since Folin (1) and others have shown that ascorbic acid and uric acid, both contained in adrenal glands, often interfered with the formation of colored compounds of epinephrine and certain metallic salts, it seemed advisable to remove them or inactivate them in adrenal extracts. Edlbacher and Leuthardt (2) state that ascorbic acid and minute amounts of copper will inactivate urease. It seemed possible to us that the reverse might also be true and that urease without the copper might inactivate ascorbic acid. Therefore, urease was added to a solution of epinephrine which also contained uric acid and ascorbic acid and the ferric ammonium oxalate was added after warming for a period of ten minutes. The bluish-violet color developed. When ferric ammonium oxalate was added to a solution containing adrenalin and ascorbic acid the color did not develop. Uric acid does not prevent the formation of the color nor does it give the color itself as it does in Folin's method. Apparently the ferric ammonium oxalate as such is not specic for the color since other ferric salts and oxalates together with adrenalin gave similar results. Ferrous salts and oxalates when added together to adrenalin, however, gave negative results.

Since the color developed by epinephrine and ferric ammonium oxalate is more stable than the color developed by Folin's method and since the sensitivity is as great or greater than that given by his method and by other methods also, and since uric acid does not interfere in our method and ascorbic acid can be blocked, we have determined the average K value of the bluish-violet compound so that the method described by us can be used for a quantitative spectrophotometric determination of epinephrine. A curve has been plotted for per cent transmission and concentration on semi-logarithmic paper using the data given in the method.

Spectrophotometric Method for the Determination of Epinephrine

To a 12.5 mg sample in 250 cc of H_2O, add 2 cc of a 10% solution of ferric ammonium oxalate ($Fe(NH_4)_3(C_2O_4)_3 \cdot 3H_2O$). Shake well and let stand for 10 to 15 minutes, then read in a spectrophotometer at 555 mμ. The average K value obtained by us from Beer's law is 8.4. Seven points plotted on semi-logarithmic paper are:

Cencentration, mg/100 cc	Transmission,
5.0	45.5
4.8	47.5
4.0	53.8
3.4	57.8
3.0	60.7
2.4	67.0
2.0	71.1

This method is accurate from less than 1% to 5% as the greatest variation. If the concentration of epinephrine is very small and the green of the reagent masks the characteristic bluish-violet color, it is advisable to use a larger sample and less of the reagent.

Uric acid does not interfere with the test, but ascorbic acid prevents the formation of the color. However, this can be avoided if 0.1 gm of urease is added to the sample in about 25 cc of H_2O and warmed for 10 minutes. Dilute to 250 cc and add the reagent. This solution can then be filtered through a fine sintered glass filter or cleared by adding $Al(OH)_3$, centrifuging and decanting.

Two compounds somewhat similar to epinephrine in structure, catechol and pyrogallic acid give a bluish color with ferric ammonium oxalate. However, they do not interfere with the quantitative determination. Other compounds such as tyrosine, quinhydrone, recorcin, orcinol, phloroglucinol and ephedrine form yellow to pink colors with the reagent, but they also do not interfere with the quantitative determination of epinephrine.

The bluish-violet color does not form in acid or basic solutions, therefore, the test is not applicable to blood since in the usual methods acid must be used in precipitating the protein.

Summary

1. A spectrophotometric method has been developed for the determination of epinephrine, which is dependent upon the formation of a blu-

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SUPPRESSION AND FACILITATION — A REVIEW

By GEORGE CLARK, Ph.D.

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IN 1936 there appeared a report (Hines, 1) still only available in abstract form, which has had a profound effect upon current trends in neurophysiology. As a result of this work or more exactly as a result of experiments based on this report, the term suppression has been added to our armamentarium and the phenomenon which it names is being used to explain decerebrate rigidity and spasticity. There is, however, no general account and since the discussions in current textbooks are at best garbled a short review seems indicated. This will be done under the following subdivisions: first a generalized account will be given which will serve as a quick survey of the field, then specific portions of that account will be examined, next two theories of decerebrate rigidity and spasticity will be discussed and, finally, a synthesis will be attempted.

Suppression is that particular form of inhibition which is concerned primarily with the halting of activity in neural tissue by stimulation of other neural tissue at a suprasegmental level. It must not be confused with reciprocal innervation in which there is inhibition of opposing activity. Suppression was first described as a cortical phenomenon and this phase should be considered first. In Figure I are shown lateral and medial views of the brain of the macaque monkey (the animal on which most studies of suppression have been made). It will be seen that five regions are delimited by dotted lines. These are the five suppressor areas: 8, 4s, 2, 19 and 24.* It should be noted that these figures are only suggestive of the actual figures of Brodmann (see Hines, 2, p. 8). Electrical stimulation or strychninization** of these bands are said to produce three types of

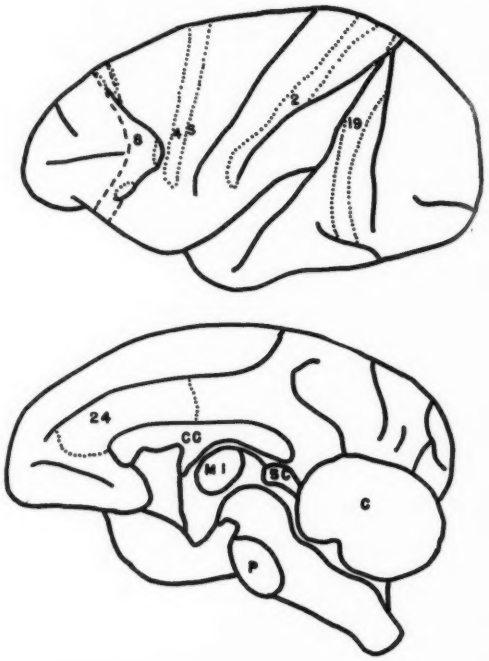

FIGURE I. Lateral and medial views of the brain of the monkey (Macaca mulatta). These were redrawn from various sources. The lateral view was combined from several figures in Volume IV of the Illinois Monographs in the Medical Sciences (1944). Two versions of area 8 are shown. The one includes only the areas enclosed by the dotted lines and the accompanying fissure while the other includes the area enclosed by the interrupted lines and the same fissure. The other suppressor bands are also enclosed by dotted lines. The medial view was redrawn from Smith (16). The following abbreviations apply to all figures: A—anterior commissure, BP—basis pedunculi, C—cerebellum, CC—corpus callosum, CG—central gray, F—facial nerve, H—hypoglossal nucleus and nerve, MI—massa intermedia, MLF—median longitudinal fasciculus, O—inferior olive, P—pons, PN—posterior column nuclei, PY—pyramidal tract, R—inferior reticular nucleus, SC—superior colliculus, T—nucleus of the spinal root of the trigeminal nerve, TS—tractus solitarius and V—vestibular nuclei.

a weak solution of strychnine to the surface of the brain or the injection of variable amounts of such a solution into subcortical structures. There results a hypersynchrony of discharge of the affected neurons which is manifest by the large potential changes that may be shown by appropriate electrical recording mechanisms. Since it produces a hypersynchrony of discharge rather than simply activation only cells and not fibers are primarily excited. The temporal dispersion of the resultant nervous impulses at synapses presumably makes it impossible to demonstrate these effects beyond the first synapse.

*There is a certain convenience in the use of the Brodmann system of nomenclature notwithstanding the fact that such an extensive subdivision of the cortex cannot be defended on histological grounds (Lashley and Clark, 3). In this paper this numbering is used to suggest approximate cortical location and certainly with no intention of implying that each of these areas is either structurally or functionally distinct.

**The strychninization method was developed by Dusser de Barenne and his associates and has been widely used by that group (McCulloch, 4) and sporadically by others. It consists in the application of small bits of filter paper soaked in

effects: (1) relaxation of any existing muscular contraction, (2) a holding in abeyance of the motor after-discharge (but not the cortical electrical after-discharge) set up by antecedent stimulation of other cortical foci, and (3) a suppression of motor response to stimulation of any motor focus.

This last is accompanied by a spreading depression of the electrical activity of the cortex. Incomplete suppression of a motor response would be indicated either by a decrease in amplitude of a response or by an increase in threshhold.

The time elements of these three differ. The first two—relaxation of an existing muscular contraction and the holding in abeyance of motor after discharge—have little or no latency while the third—suppression of a motor response—has a rather long latency which varies with the depth of anesthesia, stimulus strength and stimulus duration. No discussion of the pathways involved in the first two elements has been found but both suppression of a motor response and suppression of electrical activity of the cortex involve subcortical circuits.

Fibers pass from all the suppressor bands to two subcortical structures: the caudate nucleus and the bulbar inhibitor area. From the caudate nucleus the pathway essential for suppression of the electrical activity of the cortex passes to the thalamus and thence to the cortex. In Figure II is shown a midsagittal reconstruction of the brain stem of the monkey with the location of the bulbar inhibitory area indicated by the dotted line and in Figure III are shown four transverse sections through the bulbar reticular formation in the cat with the points from which inhibition was obtained indicated by the black circles. The exact course of the descending fibers from this bulbar inhibitory area has not been determined. However, the effects of bulbar stimulation are bilateral, the descending fibers within the spinal cord are concentrated in the medial portion of the ventral half of the lateral column and the partial crossings are entirely spinal.

No account of suppression would be complete without some consideration of facilitation, the counterpart of suppression. Outlined by the interrupted line in Figure II is an area where stimulation at a strength insufficient to produce activity by itself will augment the motor response to stimulation elsewhere, either at cortical, subcortical or even spinal levels. It will be seen that the area is practically coextensive with the

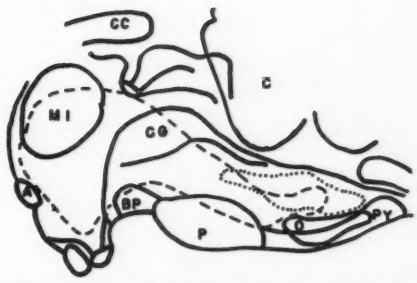

FIGURE II. Projection of the facilitatory region (enclosed by interrupted line) and inhibitory area (enclosed by dotted line) upon a median sagittal section of the brain stem of the monkey. This figure was redrawn from various sources (39, 40, 43 and 54).

reticular formation of the upper brain stem. At caudal levels it is found only in the lateral portions of the brain stem for the medial portion (see Figure III) is occupied by the inhibitory area. Descending connections from this facilitatory area are both crossed and uncrossed with the sites of crossing not exclusively spinal as in the case of the descending inhibitory fibers.

The usual decerebration interrupts the projection fibers of the suppressor areas and "denervates" the bulbar inhibitory area. The facilitatory region, however, receives impulses from the ascending sensory systems and thus its facilitatory action on the spinal internuncial pools is not seriously affected. The resultant inbalance of inhibitory and facilitatory action produces the increased extensor tonus that has been termed decerebrate rigidity. In the chronic state another facet of this inbalance is seen. The stretch reflex is unchecked by inhibitory impulses and augmented by the unopposed facilitatory impulses. The result is the triad—hyperactive deep reflexes, easily induced clonus and increased resistance to

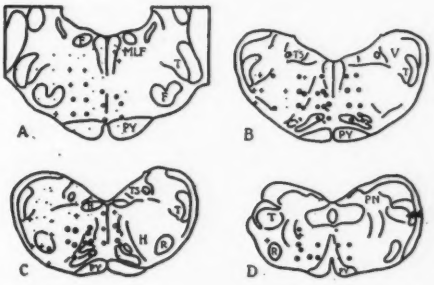

FIGURE III. Four transverse sections through the lower brain stem of the cat showing the location of bulbar points whose stimulation gave inhibitory effects (black circles) or facilitatory effects (crosses). Abbreviations as in Figure I. This figure was copied from Magoun and Rhines (39).

passive manipulation—that is collectively termed spasticity.

This abbreviated summary of suppression and facilitation seems simple and the suggestions as to their primary role in decerebrate rigidity and spasticity reasonable, however, there are widespread discrepancies in the experimental evidence. Many of these will be noted as the specific details of these two phenomena—suppression and facilitation—are discussed under the following subdivisions: (1) suppression of the electrical activity of the cortex, (2) effects of stimulation of suppressor areas, (3) effects of extirpation of of suppressor areas, (4) the pathways involved in suppression, and, finally, (5) miscellaneous remarks.

Pathways for Electrical Suppression

One of the aspects of suppression is that electrical stimulation or strychninization of any of the suppressor bands will produce a marked "flattening out" of the electrocorticogram after a latency which varies with the physiological state of the animal. This has been termed suppression of the electrical activity of the cortex. With a battery of electrodes placed on the cortex it has been shown that beginning at the area stimulated this process passes in wavelike form across the cortex so that nearby points may be recovering while more distant points are fully suppressed. It has been shown further that the contralateral hemisphere is affected as well as the ipsilateral hemisphere. This spread to the opposite hemisphere survives section of the corpus callosum. The impulses travel directly to the caudate nucleus from the stimulated point for after strychninization of small areas of any of the suppressor bands strychnine spikes may be picked up from the caudate nucleus. The reports (McCulloch, 4) indicate some localization within the caudate for area 19 projects to the tail of the caudate while 4s and 8 project to its head but exact details have never been reported.

Using the same method area 4 has been shown to project to the putamen and area 6 to the putamen and to the lateral segment of the globus pallidus but suppressor areas are said to have no direct connections with these two nuclei. These results are interesting for they would indicate that the putamen and caudate nuclei have different functions. Anatomists have long insisted that since the caudate and putamen are similar morphologically they must have similar functions and indeed they are often considered as a single structure secondarily invaded by the internal capsule. Does this indicate that such morphological evidence may be extremely misleading? The pathway from 4s to the caudate nucleus has been said to be via unmyelinated collaterals from fibers in the internal capsule (Glees, 5) that were originally described by Cajal, as Mettler (6) has said, however, the "precise limits of the cortical areas" which give rise to these fibers is not known. The remainder of the pathway is given by McCulloch (4) who stated that "the suppression of electrical activity of the cortex has been shown to depend on impulses reaching the nucleus caudatus and thence indirectly interrupting in the ventrolateral nuclei of the thalamus that regular rhythmic oscilllation of voltages between sensory cortex and thalamus without which there are no ordinary 'spontaneous' electrical waves of the sensory cortex." Marchi studies (Ranson and Ranson, 7; Glees, 8) have not demonstrated direct connection from the striatum to the ventrolateral nuclei and since intrathalamic connections are rare (Krieg, 9) there is as yet no anatomical basis for the above quoted statement. In fact, much of the pathway is hard to visualize morphologically. Commissural connections between the basal ganglia are insignificant while the "wave-like" progression of the electrical suppression across the cortex would seem to require a very complicated system of intrathalamic connections.

Summary. There are so many gaps in the data on the pathways whereby suppression of the electrical activity of the cortex is propagated that definite statements are not warranted. About all that can be said is that fibers pass from the suppressor areas to the caudate nucleus without synapse and that this nuclear mass is an essential link in the pathway but that the remainder of its course is entirely hypothetical.

Effects of Stimulation of Suppressor Areas

The principle features of the effects of stimulation of suppressor areas in anesthetized preparations have been given in the introduction. Most of these have been observed in the three reports of suppression in the human. The first case was reported by Garol and Bucy (10). The cortex of their patient, from whom portions of the motor cortex were subsequently removed for relief of persistent unilateral tremor, was stimulated with a 60 cycle sine wave stimulator under

light ether anesthesia. They report the following. Stimulation of one particular area evoked immediate relaxation of existing muscular tension in the contralateral arm (the position of the patient precluded testing other extremities). After such stimulation the threshold in the region just anterior to the central fissure was markedly increased. Also a motor after-discharge elicited by supraliminal stimulation of the motor area was abruptly stopped about 5-10 seconds after stimulation of the suppressor region. Niemeyer (11) extended these findings. In his patient he found that stimulation of a region (in the approximate position described by Garol and Bucy (10)) produced a decrease in the spontaneous electrical activity of the cortex and the disappearance of a contralateral tremor. This patient was given pentothal in addition to the local anesthesia at the time of breaking the bone flap. Hecaen, David and Talairach (12) also found that cortical stimulation could inhibit tremor and simultaneously evoke a complete loss of tonus which persisted for some time. At another point the tremor was suppressed with no effect on tonus. Again this suppressor area was located in about the same position as in the two other reports.

The report of Garol and Bucy (10) mentioned above, further complicates the question of latency of these responses. None of these reports on studies of experimental animals suggest an appreciable delay before suppressor band stimulation is able "to hold in abeyance a cortical motor after-discharge," yet Garol and Bucy (10) report a latency of 5-10 seconds. Since they confirm the usual report of prompt inhibition of existing muscular tone the difference in latency of the two responses indicates that they may have in common only the property of being elicitable from the same area and with the same stimulus. Similarly, Hecaen, David and Talairach (12) report that at one point the tremor could be inhibited without affecting muscle tone. This too, may be taken to indicate that the two responses differ in their underlying mechanisms.

Another inexplicable facet of suppression is the long and variable latency for suppression of a motor response. Where temporal summation to a tetanic stimulation or where endocrine secretion is involved latencies of a few seconds are not at all unusual but the reviewer, at least, can not visualize how the response to stimulation of a cortical area may have a latency of minutes while stimulation of the bulbar inhibitory area, which is said to be activated by impulses from the same cortical area, evokes the same response with no appreciable delay. Even if long delay paths were involved it would not be easy to understand and in this case the evidence from strychninization experiments indicates that the pathway is directly from cortex to bulbar inhibitory area with no synapses.

There are two reports of stimulation of suppressor areas in unanesthetized experimental animals. In the first of these (Clark and Ward, 13) monkeys were used. The experiment was based on the assumption that if head or head and eye movements (Bailey, Dusser de Barenne, Garol and McCullock, 14) could be evoked by stimulation of an electrode implanted in this region, then the electrode must be located on the anterior suppressor band. They found no evidence for suppression. Instead there was, as elsewhere in the region anterior to the central sulcus, potentiation of the responses evoked by consecutive or concurrent stimulation of an electrode located in the eyefields and another on a motor point. Clark, Chow, Gillaspy and Klotz (15) implanted one electrode on the limbic suppressor area and another on the motor cortex in a series of dogs. They, too, report potentiation of the responses. Instead of suppression of clonus they report convulsions from stimuli of only slightly greater strength than that necessary to induce the alterations in respiration which are so typical of this region. (Smith, 16; Ward, 17; Kremer, 18.) Under Dial anesthesia, however, they were able to elicit typical suppression. It should be noted, in connection with this failure to induce suppression in the unanesthetized experimental animal, that in their several publications on stimulation of the cortex in unanesthetized humans, Penfield and his associates make no mention of suppression.

As far as "suppressor" effects are concerned there is apparently no difference in the responses evoked by stimulation of the various suppressor bands. However, by stimulation of 8 and 19 head and eye movements may be elicited and by stimulation of the limbic suppressor band a number of different types of responses may occur. These include alterations in respiration, heart rate and blood pressure, piloerection, pupillary dilatation, vocalization, etc. Any of these may occur alone or in various combinations but there have been no suggestions as to the cause of these variations

in response. In the two papers on stimulation of this region in the monkey the suppressor effects are similar but there are discrepancies which might possibly be explained on the basis of differences in anesthesia and types of stimulating current.

One report is difficult to explain. McCulloch, Graf and Magoun (19) report that on strychninization of 4s, strychnine spikes may be picked up in the pyramidal tract and motor twitches may be seen in the contralateral limb. They suggest that these were due to the activation of cells in area 4 but fail to mention the important question of why this activity was not suppressed.

The statement has been made repeatedly, in articles on suppression, that when one traces a response point by point by "secondary facilitation" suppressor bands interfere with the procedure, for if, in so doing, these bands are stimulated, no further responses are obtainable (Dusser de Barenne, Garol and McCulloch, 20). This sounds quite reasonable but such workers have apparently failed to compare their maps with reports of secondary facilitation. Thus, Ward and Clark (21) describe such facilitation in the cat. If one compares their diagram of the course of a particular facilitation (their Figure 3) with a diagram of the suppressor bands in the cat as described by Garol (22) (his Figure 2) it is apparent that Ward and Clark (21) did carry secondary facilitation across a suppressor band. The reason for this discrepancy is not apparent but the failure of authors to consider the relevant earlier literature cannot be condoned.

Another discrepancy in reports of inhibition following cortical stimulation stems from the report of Hines (23). In this paper, which is routinely cited by workers in the field of suppression, the statement is made that stimulation of the strip area (later called 4s) produced relaxation of tonic extension while stimulation of area 6 evoked relaxation of tonic flexion. Although this reviewer has noted many citations of this paper of Hines, no other discussion of this inhibition from area 6 has been encountered. The reason is not apparent.

Summary. A consideration of the reported data on stimulation of suppressor bands does not clarify the material. Instead, there is revealed a maze of ill-digested material with many contradictions and inconsistencies. There is superficial agreement between these reports but nothing more. There can be no question that suppression of motor after-discharge, suppression of existing muscular activity, suppression of the electrical activity, suppression of the response to electrical stimulation of motor points and, in the human, suppression of tremor have been repeatedly demonstrated. The different and variable latencies of these responses, the inconsistencies in the various reports, the reported failure to obtain any evidence of suppression in unanesthetized dogs or monkeys, although suppression has been demonstrated in slightly narcotized humans, makes one wonder if we are dealing with a number of more or less related phenomena. If this is the case, superficial generalizations may well hinder further progress.

Results of Extirpation of Suppressor Areas

In a discussion of the effects of ablations of the peristriate and eyefields regions (Lashley (24) has recently stated that "The disagreement of results emphasizes the need for more detailed anatomic control of physiologic studies. Methods for analysis of cerebral lesions are still very crude. If the subjects survive for any length of time the Marchi method is inapplicable and degeneration of fibers can be identified only in large tracts. Retrograde degeneration may also become more difficult to define accurately. Nevertheless, histological examination of serial sections does provide information which cannot be obtained at operation or by gross examination at necropsy. The study of cerebral function has progressed to the point where utilization of every possible anatomic control is essential for interpretation of the data. Neither Jacobsen, Ades, nor Kennard has described the experimental lesions adequately and the significance of their results for specialization of cortical areas is equivocal." By the inclusion of more names in the last sentence of the above quotation it would apply exactly to reports on extirpation of the suppressor bands. Since it is hardly possible from the various reports themselves to determine why they differ and since the various authors have almost routinely ignored discrepancies, it is not possible to do more than record the reported deficiency syndromes and note some of the discrepancies.

While there are several reports on the results of hemidecortication or even hemispherectomy in various species there could be found only one attempt to remove in one animal all the

suppressor areas of one hemisphere (Ward, 17). In this animal (monkey) there was "minimal or no spacticity of the contralateral extremities." In the same paper various behavioral changes resulting from ablation of the limbic suppressor band are discussed and the statement is made that "there was no change in motor control, deep reflexes, muscle tone or resistance to manipulation." Lashley (24) and Ades (25) both removed in the monkey most if not all of area 19 plus additional tissue. Neither of these mention any additional tissue. None of these mention any spasticity nor, in unilateral operations, any difference in motor control of the two sides. Among those who have attempted to remove area 8 may be mentioned Mettler (26), Kennard (27) and Clark and Lashley (28). None of these mention finding spasticity, increased resistance to passive movement or any other of the numerous symptoms that one could reasonably anticipate encountering following suppressor band ablations. As mentioned earlier Ward (17) found no alterations in motor control, deep reflexes, muscle tone or resistance to passive motion although he did find various behavioral changes confirming the earlier report of Smith (29). No reports of isolated removal of the parietal suppressor band (area 2) were found but there were two recent accounts of larger ablations in this region (Peele, 30; Kennard and Kessler, 31) with fairly detailed accounts of motor performance. These two papers, while agreeing as to the initial findings, disagree as to the amount of recovery. Both found that there was at first a decrease in resistance to passive motion, a decrease in tendon reflexes and hypotonia. While both agree that the hypotonia was persistant Kennard and Kessler (31) found that the resistance to passive manipulation gradually returned to normal and that deep reflexes ultimately became hyperactive. This hyperactivity of deep reflexes is the only suggestion of any of the symptoms one could expect from suppressor band ablation.

In contrast to the other suppressor bands ablation of 4s has routinely been reported to produce alterations in motor performance. The classic descriptions of Hines (1, 23) include the following. Ablation of the strip area (4s) produces a differential muscular hypertonus which is maximal in the extensors of the knee and flexors of the elbow. Clonus is easily induced and tendon reflexes are brisk. These phenomena are bilateral although predominantly contralateral and are apparently permanent with bilateral removals. Cannon, Magoun and Windle (32) removed the "anterior border of 4 and the posterior border of 6", approximately the area removed by Hines (1936, 1937) with rather different results. They report a transient spasticity in the flexor muscles of both contralateral extremities without clonus but with permanent hyperactivity of deep reflexes. They consider their results similar to those of Kennard and Welch (33) These latter workers, however, appear to believe that removal of medial portions of area 6 is essential and they also state that this "paralysis in flexion" followed simultaneous removals only and that unilateral or seriatim ablations failed to produce the flexor posture. Unexplainedly in their smallest area 6(?) lesion there was also damage to the corpus callosum. Since there were no details as to the exact tissue destroyed or the thalamic degeneration that resulted, it would seem that repetition of the experiments would be the only way to reconcile these reports.

A very interesting finding of Kennard and McCulloch (34) and of Hines and Boynton (35) is that stimulation of 4s in the fetal monkey (Hines) or new born monkey will produce the usual suppressor effects but that ablation of 4s is not followed by spasticity. If these animals are allowed to survive, however, moderate spasticity does develop when they become about six months old. The significance of this is only conjectural except as it casts doubt on the hypothesis that spasticity is due to the denervation of the structure whose excitation produces suppression.

There are several reports of Mettler (6, 26, 36, 37) and of Hines (2, 23) which should be read in the originals. As the work of the initiator of these studies on suppression, the reports of Hines warrants consideration. In addition the logical organization and the inclusion of much otherwise unreported material makes them extremely valuable. Mettler's reports include a wealth of physiological data and, in welcome addition, sufficient anatomical data to enable one to have a fair idea of the extent of most of the lesions. Only a few features of these papers can be mentioned. The expected signs of suppressor band ablation—hyperactive deep reflexes, clonus and increased resistance to passive motion—were found after removal of 4s but the severity and duration of these symptoms increased as additional tissue

was removed. Thus, the result of complete frontal lobectomy (sparing 24?) which means of course the removal of much non-suppressor band tissue in addition to 4s and 8, was a marked increase in severity of symptoms as compared with simple 4s ablations. Mettler (37) too, has insisted on and presented adequate evidence to prove that removal of basal ganglia in addition to even a complete hemidecortication increases the severity of the suppressor band syndrome.

On the basis of the general theory given in the introduction the above results are hard to understand. Since all the suppressor bands project on the bulbar inhibitory area and the results of their stimulation (at least with regard to lower motor neurons) are interpreted in terms of the activation of the bulbar inhibitory area, the results of their ablation should thus be explicable in terms of denervation of the bulbar inhibitory area. How can it be possible, under these conditions, for removals of 8, 19, 24 and 2 (except for the hyperreflexia in one of two reports) to precipitate none of the phenomena that are seen following removal of the other suppressor band (4s)? Moreover, how can ablation of 4s be followed in one case by extensor rigidity and in another by flexor rigidity? And further, how can one account for the lack of effect following removal of all the suppressor bands by Ward (17)? Also how can removal of nonsuppressor areas increase the effects of suppressor removal? The extent to which these questions will be reconciled when the studies are repeated with adequate anatomical control is problematical, but espousing one position and ignoring the inconsistencies will not advance cortical physiology.

Summary. It is possible that when a large variety of cortical ablations are made which are adequately controlled anatomically and carefully studied physiologically, it will be possible to reconcile the many discrepancies in the reports of deficiency syndromes. It is only possible to state that at present there is insufficient evidence to confirm what could reasonably be expected from the general theory given in the introduction.

Pathways of Suppression and Facilitation

Specific information on the pathways involved in suppression and in facilitation of motor responses are limited to a few papers but there is a myriad of reports dealing with the pathways involved in spasticity and with decerebrate rigidity. It would be impossible and perhaps pointless, to cite each of this latter group for usually the anatomical details of the extent of the lesions and the pathways destroyed are not given. Some will be considered, however, which pose interesting questions or which suggest a means of approach to the problem. Dusser de Barenne and McCulloch (38) studied the effect of various subcortical ablations on the suppression produced by stimulation of 4s. They found that the following structures were severally unnecessary for the occurence of suppression: putamen, caudate nuclues, globus pallidus, thalamus, substantia nigra and cerebellum. McCulloch, Graf and Magoun (19) used the stereotaxic instrument to orient electrodes in an attempt to pick up subcortically the strychnine spikes following strychninization of areas 4s. Apparently they studied only the distribution of potentials in the medulla and lower pons. They found that the region from which these strychnine spikes could be recorded was coextensive with the bulbar inhibitory area (Magoun and Rhines, 39). At that time they found evidence only for descending connections from the ipsilateral cortex. Unexplainedly they mention recording strychnine spikes from the pyramidal tract and mention that motor twitches of the contralateral limbs were present "at the height of activity." This is a surprising statement for one would assume that such twitches would have been completely suppressed. Later Magoun and Rhines (40) apparently found descending connections from the contralateral hemisphere as well. Do these findings indicate that negative findings by the strychnine method, as in the Marchi method, are only of suggestive value? McCulloch, Graf and Magoun (19) also attempted to determine at what point this descending pathway diverged from the pyramidal tract. While strychnine spikes were recorded from the bulbar inhibitory area after section of one of the pyramids at the caudal border of the pons, a similar section of the basis pedunculi at the rostral border of the pons eliminated the spiking although they were still present on the contralateral side following strychninization of the opposite area 4s. In the latter case, the most medial portion was intact. This was taken to indicate that the fibers from 4s diverged from the descending corticospinal tract in the pons. Since it has been shown by Cannon, Magoun and Windle (32) that the "fibers whose interruption is responsible for the phenomenon of hypertonicity and those dealing

with clonus, for the most part, have deviated from the corticospinal projection prior to reaching cerebral peduncle," should this be taken to mean that the descending connections from 4s are responsible only for hyperreflexia? Each of these findings is also hard to correlate with the report of Weed (41) that stimulation of the mesial 1/5 of the basis pedunculi inhibited decerebrate rigidity for this is approximately the portion left intact by McCulloch, Magoun and Graff (19) in their lesion at the anterior border of the pons Verhaart and Kennard (42), using the Marchi method, traced fibers from 4s through the internal capsule, basis pedunculi to the homolateral pons. Hines (2) confirmed this projection to the pontile tegmentum and also traced pyramidal fibers from 4s to the contralateral spinal cord. One conjectures whether the difference in results might have been due either to poor impregnation with osmic acid or to the cortical lesions involving more than 4s. By electrical stimulation of the bulbar inhibitory area after placing appropriate spinal lesions, Niemer and Magoun (43) demonstrated that the descending pathway was widely distributed in the ventral and lateral funiculi of of the spinal cord with a concentration in the ventral portion of the lateral column. A similar localization was reported for the pathway concerned with decerebrate rigidity by Liddell, Matthes, Oldberg and Ruch (44). As stated by Magoun and Rhines (40) this agrees in many respects with the reports of Hyndman (45) and of Putman (46) in man, and of Wagley (47) in the monkey. However, these reports do not agree too well in some details. For example, Wagley's monkey W_1L had hyperreflexia following a partial lesion of the ventral funiculus while in others with lateral column lesions the prominent symptom was an increased resistance to passive motion. The lesion in Wagley's monkey W_5L, which had brisk tendon reflexes and increased resistance to passive motion was located, as near as can be determined, entirely within the portion of the lateral column found unessential for either facilitation or inhibition of motor responses by Niemer and Magoun (43). The reason for these discrepancies is not clear. They could be taken either to indicate wide individual differences in location of descending pathways or to suggest the possibility that several different processes are concerned.

Inhibition of cortically induced or spontaneous movements has also been reported from stimulation of the striatum. Since there is no data on the descending pathways involved the relationship between this striatal inhibition and suppression is problematical. Mettler (36) has recently summarized this material. Stimulation of practically all parts of the caudate nucleus and putamen resulted in the inhibition of cortically induced or of spontaneous movements. The effects are bilateral and there is no indication of somatopical localization. In some reports Mettler and his associates (48, 49) indicate that movements contralateral to the nucleus stimulated are more easily inhibited while Freeman and Krasno (50) found the effect more marked ipsilateral to the nucleus stimulated. The later also report autonomic effects which may indicate that the suppressor system of McCulloch and Magoun are not concerned. It should be stressed that this striatal inhibition of movement is induced by stimulation of both the caudate nucleus and the putamen which make it unlikely that it bears any relation to the suppression of electrical activity of the cortex in which the putamen plays no part.

It has long been known that stimulation of the anterior lobe of the cerebellum would produce relaxation in the extended limbs of a decerebrate preparation. This is now being actively investigated and several of the more important papers are still available only in abstract form. Although there is information indicating that the cerebellar suppressor and facilitatory system act through the bulbar inhibitory area and the reticular facilitatory region, the fact that there is some evidence of somatopical localization and the presence of antonomic effects make it necessary to reserve judgment until more information is available.

Relaxation of existing muscular tension has been reported to have been evoked by cortical stimulation too weak to induce movement. This has been noted in the anesthetized cat (Tower, 51) and in the unanesthetized monkey (Clark and Ward, 52). In view of the internuncial inhibitory theory of Brooks and Eccles (53) any relation of such relaxation to suppression is questionable.

As noted in the introduction the facilitatory region as outlined by Rhines and Magoun (54) includes practically all the reticular formation not included in the inhibitory area. Stimulation of points within this area, with a stimulus strength subliminal for motor responses, was

found to potentiate the response to stimulation of motor cortex, bulbar pyramid, peripheral nerves, etc. Niemer and Magoun (43) have shown that in the spinal cord the descending connections from this facilitatory region are distributed similarly to those from the bulbar inhibitory area but extend slightly farther ventrally. Potentiation of responses to stimulation of fibers in the pyramids by concurrent excitation of the facilitatory region continued after an acute decortication (Rhines and Magoun, 54). This was taken to indicate that the site of facilitation lay at the level of the lower motor neuron. However, this concept, that the connections from the facilitatory region are entirely descending may not, perhaps, be correct. The experiments of Rhines and Magoun (39) certainly rule out the possibility that the site of facilitation is solely cortical but they do not rule out the possibility that both descending and ascending connections exist. Ranson (55) for example, found it necessary to assume ascending connections from the anterior portion of the facilitatory region in order to explain the hypersomnelence he found in a series of monkeys. Lacking this "upward drive" or in other words, the constant play of facilitatory impulses from hypothalamus to cortex, the monkeys were sleepy. The pathway he assumed from hypothalamus to thalamus to cortex is the same assumed by Murphy and Gellhorn (56) to explain the potentiation of responses to cortical stimulation by subliminal excitation of the hypothalamus. Certainly facilitation at a cortical level does exist, for Clark and Ward (13), describe augmentation of responses by concurrent or consecutive stimulation of two cortical points in unanesthetized monkeys.

The low frequency pyramidal discharges studied by Adrian and Moruzzi (57) has been suggested (Magoun and Rhines, 40) as the basis for the hypotonia resulting from area 4 ablations (see Mettler, 26 for literature and confirmation) section of the basis pedunculi (Cannon, Magoun and Windle, 32) the bulbar pyramid (Tower, 58) and the lateral corticospinal tract (Wagley, 47). This, then, would be a second facilitatory pathway and a second facilitatory mechanism. Whatever may be the explanation for these reported hypotonicities the possibility should be considered that they are not related. Recently, Liddel and Phillips (59) have reinvestigated the effects of section of the pyramidal tract. They took especial care to damage the blood supply as little as possible and ascribe their results to their operative technic. They were able to routinely demonstrate hypertonia in the cat with sectioned pyramids. However, in those animals in which additional damage occurred hypotonia not hypertonia was found. Since Tower's findings in the monkey (58) duplicated her findings in the cat (60) it might be predicted that extensor rigidity would result from uncomplicated pyramidal section in the monkey. If so, this would eliminate the possibility that the loss of the low frequency discharges studied by Adrian and Moruzzi (57) were responsible for the hypotonicity from area 4 lesions. It would also indicate the need for considering another inhibitory pathway. Incidentally, the complicated fiber spectrum of the pyramidal tract (Lassek and Rasmussen, 61, Lassek, 62) certainly suggests the possibility that the pyramidal tract is much more than simply an initiator of willed movements.

Another facilitatory influence is provided by the vestibular system. This will be discussed in more detail later in connection with the Ward theory of decerebrate rigidity. It suffices to mention here that the vestibular system, while it may have as yet undiscovered connection with the bulbar inhibitory area and the reticular facilitatory region, has its own effect on the spinal internuncial pools and impulses over this system are essential for the maintenance of decerebrate rigidity. While we have some knowledge of the interrelationship between the vestibular system and the flocculonodular lobe of the cerebellum, the part that the vestibular system plays, if any, in the interplay between cerebellum and facilitatory reticular system remains to be discovered.

Ward (63) has recently reviewed a few of the older papers on the course of the tract (or tracts) whose interruption precipitates decerebrate rigidity. Many of these lack anatomical detail and in few of them is there any indication of any other than a gross inspection of the lesions so their evidence is largely suggestive. They unite, however, in indicating that most of the fibers decussate between the superior and inferior colliculi. This decussation is definitely below the level of the decussation of the pathway whose interruption resulted in homolateral exaggeration of reflexes (Mettler and Zimmerman, 63). The extent of the decussation is also hard to reconcile with the strychninization experiments. The apparent

lack of agreement in these findings is also contrary to the generalizations given in the introduction to this paper.

Ward (64) has also attributed the atonia following transection through the cephalic pons (Keller, 65) as directly due to destruction of the facilitatory region. This is hardly consistent with the remainder of the paper cited for Keller (65) also reported that after lateral transverse lesions in the pons, which would damage the facilitatory region and probably leave intact the inhibitory area, tone and postural reflexes are unaltered while a section which spares the lateral tegmental area, when in cephalic pons, produces an atonia similar to that of the complete transaction. This latter finding is very hard to reconcile with some of Ward's (64) experiments where he placed lesions in the tegmentum with the stereotaxic instrument. The only conclusion possible is that these apparently discordant facts suggest the need for further work.

This review of the pathways involved in suppression and facilitation has disclosed three trends which should be stressed. First, there are a number of inconsistencies which must be reconciled before any comprehensive theory can be elaborated. Second, the separation of the elements of the triad of spasticity—clonus, hyperreflexia and increased resistance to passive motion—by lesions at several different levels poses the question as to whether one mechanism can be responsible for each. And finally, the possibility has been raised that there may be several facilitatory and inhibitory pathways and thus the probability of several different mechanisms.

Miscellaneous Remarks

It was stated in the introduction that theoretical explanations of decerebrate rigidity and spasticity had been developed which attempted to explain these phenomena solely on the basis of suppressor and facilitatory systems. These theories—decerebrate rigidity (Ward, 64) and spasticity (Magoun and Rhines, 40)—will now be considered on the basis of the material covered in this review.

Ward's (64) studies of the effects of NaCN poisoning led him to attempt to integrate the suppressor and facilitatory effects into a theory explaining decerebrate rigidity. He stated "The hypothesis is advanced that both NaCN and appropriate lesions in the midbrain produce decerebrate rigidity by interrupting all afferent impulses to the bulbar suppressor region, thereby causing a deprivation-paralysis of that structure. The facilitatory region in the lateral pontile tegmentum, however, continues to receive afferent impulses from the cranial nerve nuclei as well as from the cord, and thus its facilitatory influence on the internuncial pools of the ventral horns of the cord continues unchecked. The balance between inhibitory and facilitatory impulses arriving in the cord is thereby upset. In the absence of impulses from the suppressor region in the bulb, this internuncial activity is greatly increased and is manifested peripherally as extensor rigidity." While this was a rather bold generalization, it appeared to have considerable merit and it certainly correlated a great maze of data. It was amenable, however, to experimental analysis and the following year, Bach and Magoun (66) conclusively demonstrated that it was only partially correct. This was done by comparing the effects of lesions of the reticular facilitatory system with those of the vestibular system. Section in the brainstem or in the spinal cord of descending fibers from the facilitatory reticular formation produced a transient disappearance or diminution of the extensor rigidity in decerebrate cats which was followed by a return to the original rigid state. Destruction of the vestibular nuclei (confirming Fulton, Liddell and Rioch, 67) or their descending connections terminated the rigidity. Bach and Magoun (66) very conservatively concluded that "while facilitatory reticulo-spinal connections contribute to the maintenance of decerebrate rigidity, they are not able, acting alone, to maintain it nor is their action essential for its maintenance, as is that of the vestibulo-spinal system."

In a recent monograph, Magoun and Rhines (40) have attempted to integrate the suppressor and facilitatory systems with the stretch reflex into a general theory of spasticity. Their thesis is that the spastic state is simply the result of the loss of impulses from the bulbar inhibitory area which ordinarily hold in check the stretch reflex while impulses from the facilitatory reticular formation still serve to augment the stretch reflex. The bulbar inhibitory area is therefor only a relay center for the cortical suppessor areas while the facilitatory areas may be activated by ascending sensory fibers. This theory is probably an overgeneralization. It fails to account for the following: (1) Ablation of only one

of the suppressor areas (4s) results in the symptomatology demanded by the theory, (2) Ablation of all the suppressor bands eliminates even the spasticity which follows ablation of 4s alone, (3) Ablation of nonsuppressor areas augments the spasticity resulting from 4s removals, (4) Hemidecortication but not unilateral removal of all suppressor bands produces spasticity, (5) Spasticity of cortical origin is enhanced by subcortical lesions, (6) Accounts of the pathways involved are inconsistent, (7) How can the various elements of the triad of spasticity be separated by appropriate lesions at all levels, both above and below the reticular facilitatory and inhibitory systems? (8) How can the findings of extensor rigidity following section of the pyramids be reconciled with the theory? and finally, (9) There is the question of the identity of spacticity and augmented stretch reflexes. As Kennard has stated (68), heightened stretch reflexes are ordinarily assumed to be the cause of spasticity but as she has also stated, it is difficult to explain hyperreflexia in a limb which shows diminished resistance to passive motion on such a basis. Similarly, it is difficult to explain the dorsiflexion of the wrist of the hemiplegic spider monkey or flexor rigidity after cortical lesions. While there is much provocative material in their discussion, and while there can be no doubt that the facilitatory and suppressor systems studied by Magoun and Rhines (40) probably play an important part in spasticity, the theory does not seem to account for all the facts.

It is interesting to speculate on the lead supplied by Bach and Magoun (66), who, as mentioned earlier, conclusively demonstrated that decerebrate rigidity was not due solely to an imbalance produced by a denervated inhibitory area in the presence of a virtually intact facilitatory region. This suggests the idea that perhaps the triad of spasticity—hyperreflexia, easily induced clonus and increased resistance to passave flexion—and are not due solely to a similar imbalance augmenting the stretch reflex. If so, what evidence is there for other systems which might also play a role. There are several of these. Magoun and Rhines (40) as noted earlier, accept the findings of Adrian and Moruzzi (57) and suggest that this could conceivably represent a second facilitatory system loss of which might account for the flaccidity following area 4 lesions. The "upward drive" of Ranson (55) by hypothalamic impulses to the thalamus and cortex may well represent a third facilitatory system. There is possibly no connection but this third facilitatory system might afford the basis for the decrease in spasticity (perhaps better the more facil use of spastic muscles) commonly seen in both the emotionally excited experimental animal and certain spastic humans (Franz, 69). Also as mentioned earlier, the finding by Liddell and Phillips (59), of increased extensor tonus as a result of pure pyramidal section must be seriously considered. This suggests a second inhibitory pathway. Further, the inhibition of movement by striatal stimulation (which may or may not be through the bulbar inhibitory area) correlates well with the report of Liddell and Phillips (70) of an increase in extensor tone after striatal lesions. Although it should be kept in mind that, since contrary reports have been made, it requires confirmation. The striking increase in spasticity afforded when striatal lesions (Mettler, 37) are added to a cortically induced spasticity may represent the confirmation. At least, however, there is a striatal suppressor mechanism whose descending pathway is not known and which may represent a third inhibitory pathway. It might also be mentioned that the connections of the various suppressor bands with the caudal portion of the cingular region has never been studied functionally and may be important. If these different facilitatory and inhibitory systems play upon different spinal internuncial pools or upon different portions of spinal reentry circuits, their action upon the lower motor neuron might well be the summation of their separate actions and one could anticipate the discrepancies found in attempting to cast them all into the one mold.

BIBLIOGRAPHY

1. Hines, Marion. *The anterior border of the monkey's (Macaca mulatta) motor cortex and the production of spasticity.* Amer. J. Physiol., 116:76, 1936.

2. Hines, Marion. *Control of movements by the cerebral cortex in primates.* Biol. Rev., 18:1-31, 1943.

3. Lashley, K. S., and George Clark. *The cytoarchitecture of the cerebral cortex of Ateles: A critical examination of architectonic studies.* J. Comp. Neurol., 85:223-305, 1946.

4. McCulloch, W. S. *The functional organization of the cerebral cortex.* Physiol. Rev., 24:390-407, 1944.

5. Glees, P. *The anatomical basis of cortico-striate connections.* J. Anat., 78:44-51, 1944.

6. Mettler, F. A. *Extracortical connections of the primate frontal cerebral cortex. II. Corticofugal connections.* J. Comp. Neurol., 86:119-166, 1947.

the corpus striatum. Res. Publ. Ass. nerv. ment. Dis., 21:

7. Ranson, S. W., and Ranson, S. W. Jr. *Efferent fibers of* 69-76, 1941.

8. Glees, P. *The interrelations of the striopallidum and the thalamus in the macaque monkey.* Brain 68:331-347, 1945.

9. Krieg, W. J. S. *Personal communication.* 1949.

10. Garol, H. W., and Bucy, P. C. *Suppression of motor response in man.* Arch. Neurol. and Psychiat., 51:528-532, 1944.

11. Niemeyer, Paulo. *Supressao da resposta moterae da atividade cortical eletrica no homen.* Arq. Neuro-Psiquiat., 4:109-117, 1946.

12. Hecaen, H., M. David and J. Talaivach. *L'Aire suppressive du cortex premoteur chez l'homme.* Rev. Neurol., 76:726-732, 1947.

13. Clark, George and J. W. Ward. *In preparation.* 1949.

14. Bailey, P., J. G. Dusser de Barenne, H. W. Garol and W. S. McCulloch. *Sensory cortex of chimpanzee.* J. Neurophysiol., 3:469-485, 1940.

15. Clark, George, K. L. Chow, Carrie Gillaspy and Donald Klotz. *In preparation.* 1949.

16. Smith, W. K. *The functional significance of the rostral cingular cortex as revealed by its response to electrical excitation.* J. Neurophysiol., 8:241-255, 1945.

17. Ward, A. A. Jr. *The cingular gyrus: area 24.* J. Neurophysiol., 11:13-24, 1948.

18. Kremer, W. F. *Autonomic and somatic reactions induced by stimulation of the cingular gyrus in dogs.* J. Neurophysiol., 10:371-378, 1947.

19. McCulloch, W. S., C. Graf and H. W. Magoun. *A cortico-bulbo-reticular pathway from area 4-s.* J. Neurophysiol., 9:127-132, 1946.

20. Dusser de Barenne, J. G., H. W. Garol and W. S. McCulloch. *The "motor" cortex of the chimpanzee.* J. Neurophysiol., 4:287-303, 1941.

21. Ward, J. W., and Sam L. Clark. *Specific responses elicitable from subdivisions of the motor cortex of the cerebrum of the cat.* J. Comp. Neurol., 63:49-64, 1935.

22. Garol, H. W. *The functional organization of the sensory cortex of the cat, II.* J. Neuropath and exp. Neurol., 1:320-329, 1942.

23. Hines, Marion. *The "motor" cortex.* Bull. Johns Hopk. Hosp., 60:313-336, 1937.

24. Lashley K. S. *The mechanism of vision: XVIII. Effects of destroying the visual "associative areas" of the monkey.* Gen. Psychol. Monog., 37:107-166, 1948.

25. Ades, H. W. *Effects of extirpation of parastriate cortex on learned visual discrimination in monkeys.* J. Neuropath. and Exp. Neurol., 5:60-65, 1946.

26. Mettler, F. A. *Physiologic effects of bilateral simultaneous frontal lesions in the primate.* J. Comp. Neurol., 81:105-136, 1944.

27. Kennard, M. A. *Alternations in response to visual stimuli following lesions of frontal lobe in monkeys.* Arch. Neurol. and Psychiat., 41:1153-1165, 1939.

28. Clark, George and K. S. Lashley. *Visual disturbances following frontal ablations in the monkey.* Anat. Rec., 97:326, 1947.

29. Smith, W. K. *The results of ablation of the cingular region of the cerebral cortex.* Fed. Proc. 3:42-43. 1944.

30. Peele, T. L. *Acute and chronic parietal lobe ablations in monkeys.* J. Neurophysiol., 7:269-286, 1944.

31. Kennard, M. A., and M. M. Kessler. *Studies of motor performance after parietal ablations in monkeys.* J. Neurophysiol., 3:248-257, 1940.

32. Cannon, B. W., H. W. Magoun and W. F. Windle. *Paralysis with hypotonicity and hyperreflexia subsequent to section of the basis pedunculi in monkeys.* J. Neurophysiol., 7:425-437, 1944.

33. Welch, W. K., and M. A. Kennard. *Paralysis in flexion and tremor in the monkey following cortical ablation.* J. Neurosurg., 1:258-264, 1944.

34. Kennard, M. A., and W. S. McCulloch. *Excitability of cerebral cortex in infant Macaca mulatta.* J. Neurophysiol., 5:231-34, 1942.

35. Hines, Marion and E. P. Boynton. *The maturation of "excitability" in the precentral gyrus of the young monkey (Macaca mulatta).* Contrib. Embryol. Carnegie Inst., 28: 309-451, 1940.

36. Mettler, F. A. *Relation between pyramidal and extrapyramidal function.* Ass. Res. Ner. Ment. Dis., 21:150-227, 1942.

37. Mettler, F. A. *Extensive unilateral cerebral removals in the primate; physiologic effects and resultant degeneration.* J. Comp. Neurol., 79:185-245, 1943.

38. Dusser de Barenne, J. G., and W. S. McCulloch. *Suppression of motor response obtained from Area 4 by stimulation of area 4s.* J. Neurophysiol., 4:311-323, 1941.

39. Magoun, H. W., and R. Rhines. *An inhibitory mechanism in the bulbar reticular-formation.* J. Neurophysiol., 9:165-171, 1946.

40. Magoun, H. W., and R. Rhines. *Spasticity, the stretch reflex and extra-pyramidal systems.* Charles C. Thomas, Springfield, Ill. 1947.

41. Weed, L. H. *Observations upon decerebrate rigidity.* J. Physiol., 48:205-227, 1914.

42. Verhaart, W. J. C., and M. A. Kennard. *Corticofugal degeneration following thermocoapuation of areas 4, 6 and 4-s in Macaca mulatta.* J. Anat., 74:239-254, 1940.

43. Niemer, W. T., and H. W. Magoun. *Reticulo-spinal tracts influencing motor activity.* J. Comp. Neurol., 87:367,-379, 1947.

44. Liddell, E. G. T., K. Matthes, E. Oldberg and T. C. Ruch. *Reflex release of flexor muscles by spinal section.* Brain 55:239-246, 1932.

45. Hyndman, O. R. *Physiology of the spinal cord. I. Role of the anterior column in hyperreflexia.* Arch. Neurol. and Psychiat., 46:695-703, 1941.

46. Putnan, T. J. *Treatment of unilateral paralysis agitans by section of the lateral pyramidal tract.* Arch. Neurol. and Psychiat., 44:950-976, 1940.

47. Wagley, P. F. *A study of spasticity and paralysis.* Bull. Johns Hopk. Hosp., 77:218-273, 1945.

48. Mettler, F. A., Ades, H. W., Lipman, Eli and E. A. Culler. *The extrapyramidal system, an experimental demonstration of function.* Arch. Neurol. and Psychiat., 41: 984-995, 1939.

49. Mettler, F. A., and C. C. Mettler. *Role of the neostriatum.* Amer. J. Physiol., 133:594-601, 1941.

50. Freeman, G. L., and L. Krasno. *Inhibitory functions of the corpus striatum.* Arch. Neurol. and Psychiat., 44: 323-327, 1940.

51. Tower, S. S. *Extrapyramidal action from cat's cere-*

bral cortex: motor and inhibitory. Brain, 59:408-444, 1936.

52. Clark, George and J. W. Ward. *Responses elicited from the cortex of monkeys by electrical stimulation through fixed electrodes.* Brain, 71:332-342, 1948.

53. Brooks, C. McC., and Eccles, J. C. *An electrical hypothesis of central inhibition.* Nature, 159:760-764, 1947.

54. Rhines, R., and H. W. Magoun. *Brain stem facilitation of cortical motor response.* J. Neurophysiol. 9:219-229, 1946.

55. Ranson, S. W. *Somnolence caused by hypothalamic lesions in the monkey.* Arch. Neurol. and Psychiat., 41:1-23, 1939.

56. Murphy, J. P., and E. Gellhorn. *The influence of hypothalamic stimulation on cortically induced movements and on action potentials of the cortex.* J. Neurophysiol., 8:341-364, 1945.

57. Adrian, E. D., and G. Moruzzi. *Impulses in the pyramidal tract.* J. Physiol., 97:153-199, 1939.

58. Tower, S. S. *Pyramidal lesion in the monkey.* Brain, 63:36-90, 1940.

59. Liddell, E. G. T., and C. G. Phillips. *Pyramidal section in the cat.* Brain, 67:1-9, 1944.

60. Tower, S. S. *Dissociation of cortical excitation from cortical inhibition by pyramid section and syndrome of that lesion in cat.* Brain, 58:238-255, 1935.

61. Lassek, A. M., and G. L. Rasmussen. *The human pyramidal tract. A fiber and numerical analysis.* Arch. Neurol. and Psychiat., 42:872-876, 1939.

62. Lassek, A. M. *The human pyramidal tract. IV. A study of the nature, myelinated fibers of the pyramid.* J. Comp. Neurol., 76:217-225, 1942.

63. Mettler, F. A., and F. T. Zimmerman. *Homolateral reflex exaggeration after brain-tem lesion.* J. Comp. Neurol., 78:113-128, 1943.

64. Ward, A. A. Jr. *Decerebrate rigidity.* J. Neurophysiol., 10:89-104, 1947.

65. Keller, A. D. *Generalized atonia and profound dysreflexia following transection of the brain-stem through the cephalic pons.* J. Neurophysiol., 8:273-288, 1945.

66. Bach, L. M. N., and H. W. Magoun. *The vestibular nuclei as an excitatory mechanism for the cord.* J. Neurophysiol., 10:331-337, 1947.

67. Fulton, J. F., E. G. T. Liddell and D. M. K. Rioch. *The influence of unilateral destruction of the vestibular nuclei upon posture and the knee-jerk.* Brain, 53:327-343, 1930.

68. Kennard, M. A. *Somatic functions.* Ill. Monogr. Med. Sci., 4:243-276, 1944.

69. Franz, S. I. *Nervous and mental re-education.* The Macmillan Co., New York, 1923.

70. Liddell, E. G. T., and C. G. Phillips. *Striatal and pyramidal lesions in the cat.* Brain, 69:264-279, 1946.

SEMINARS

Held in Amphitheater A at 1:00 P.M.

January 12 "The Thumb—An Index of Phylogenetic Development." Dr. D. A. Willis, Associate Professor of Surgery, The Chicago Medical School.

January 19 "Surgery for Congenital Abnormalities of Heart and Great Blood Vessels." Dr. Egbert H. Fell, Clinical Associate Professor of Surgery, (Rush), University of Illinois.

January 26 "Physiological Problems at High Altitudes." Dr. William V. Whitehorn, Assistant Professor of Applied Physiology, University of Illinois.

February 2 "The Mechanism of Bacterial Transmutation and its Implication in Medical Research." Dr. Paul H. Kopper, Instructor in Bacteriology and Public Health, The Chicago Medical School.

February 9 "Recent Developments in the Physiology of the Frontal Lobes." Dr. George Clark, Associate Professor of Neuroanatomy, The Chicago Medical School.

February 16 "Art Treasures of the Chicago Art Institute." Mr. Peter Pollock, Public Relations Counsel, Art Institute of Chicago.

February 23 "The Significance of the Glucose Tolerance Curve." Dr. Piero P. Foa, Associate Professor of Physiology and Pharmacology, the Chicago Medical School.

March 2 "The Field of Social Pathology as Related to Medicine." Mr. Peter P. Klassen, Assistant Professor of Social Science, University of Illinois.

April 13—"The Chemist as an Aid in the Detection of Crime." Dr. Wm. D. McNally, Consultant in Toxiolcogy, Former Deputy Coroner, Toxicologist and Chief Chemist, Coroner's Office, Chicago, Illinois.

April 20—"Visual Education in Medicine." Prof. T. Jones, Chairman of the Department of Medical Instruction, University of Illinois College of Medicine, Chicago, Illinois.

April 27—"The Sedimentation Rate — Its Possible Mechanism and Its Clinical Significance." Dr. D. H. Atlas, Assistant Professor of Medicine, Chicago Medical School, Chicago, Illinois.

May 4—"The Essential Differences Between the Two Halves of the Colon." Dr. Manuel Lichten-

(Continued on page 40)

School And Faculty Notes

Dr. Jo Rogers Hood, '36, announces the removal of his office from 118 So. 80th Street to 811 So. 20th Street, Birmingham, Alabama.

It's a girl, Elaine Markoutsas, born to Dr. and Mrs. G. C. Markoutsas, '40, on November 24, 1948.

Dr. and Mrs. Joseph Liebross, '42, proudly announce the birth of Burton Alexander on Thanksgiving Day, November 25, 1948. What a happy holiday that was!

The office of S. M. Lilienfeld, M.D., '43, is now located at 22-79 Mott Avenue, Far Rockaway, N.Y.

Dr. and Mrs. A. Howard, '43, have given their four-year-old son a playmate, namely, Ronda Lyn, born December 8, 1948.

John Arthur Reinitz was born to Dr. and Mrs. Arthur Henry Reinitz, '47, on December 12, 1948.

Dr. Gordon Campbell, '47, has had to have extensive surgery followed by plastic surgery. We are glad to know that he is improving and wish him the best of good fortune in starting his practice again.

Best of luck to Harold Dorin of the Freshman Class, who was married in Chicago to Miss Virginia Fosdyke on January 22, 1949.

Stuart Cohn, a more patient Freshman, will wait until June before he makes his fiance, Miss Carola Jacobson, his bride.

The staff of **The Quarterly** joins the Freshman Class in congratulating Mr. and Mrs. Nelson Rangell on the birth of a son, Andrew Reed Rangell, December 22, 1948.

* * *

DEPARTMENT OF PHYSIOLOGY AND PHARMACOLOGY

Two research assistants have joined the staff of the Department of Physiology and Pharmacology. Mr. Sherwin Zalman will assist Dr. B. B. Blivaiss in his experiments on:

a) the toxicity of di-hydrogenated ergot; and
b) the ganglionic effects of thiamine and curare.

Mr. Jack Handel will be asociated with Dr. A. H. Ryan who is at present studying the effects of drugs on the nervous system.

A paper by Drs. P. P. Foa, J. A. Smith and Miss H. Weinstein entitled "Curare-like Action of Thiamine" was published in the October 15, 1948, issue of **Science.**

A paper on experimental work on "The Lipids of the Rat Brain and Liver in Choline Deficiency" by Dr. Foa, Miss Weinstein and Mr. Bernard Kleppel was published in the November 1948 issue of the **Archives of Biochemistry.**

Drs. Smith, Foa, Miss Weinstein, Messrs. A. S. Ludwig and J. M. Wertheim published a paper discussing some "Aspects of Thiamine Toxicity" in the July 1948 issue of the **Journal of Pharmacology and Experimental Therapeutics.** Phases of this work included the effects of thiamine on the intact animal, the effects of thiamine on the vascular system and the effects of thiamine on the heart.

Dr. J. A. Smith reports that the Sandoz Pharmaceutial Company of Basle, Switzerland, and New York City has awarded him a research grant of $600. This grant was allotted for investigation in the use of the Warburg Apparatus. Increased knowledge of this apparatus is necessary for experimental work on the influence of thiamine and insulin in vitro metabolism, and for the study of the effects of digitalis on the metabolism of embryonic hearts.

Dr. Pierro Foa will conduct an elective course on the "Physiology of Symptoms."

DEPARTMENT OF BACTERIOLOGY AND PUBLIC HEALTH

A paper by Dr. Irwin S. Nieman and Miss Nelda Holmgren entitled "A Comparison of the Immunogenicity for Guinea Pigs of BCG Cultured Intermittently and Continuously in the Presence of Bile," was published in the January 1949 issue of the **American Review of Tuberculosis.**

Dr. Ernest Hartman presented a paper on "Differential Staining" at the December 1948 meeting of the Society of American Parasitologists.

Dr. I. S. Nieman, Chairman of the Department of Microbiology and Public Health, announced that an elective course in "Virology" will be conducted in the near future. The course will be of the seminar type and will place emphasis on the newer diagnostic methods in Virology.

DEPARTMENT OF OTOLARYNGOLOGY

Roland M. Loring, M.D., announces the opening of his office for the practice of eye, ear, nose and throat at 25 E. Washington St., Chicago.

DEPARTMENT OF ANATOMY

Dr. Leon Henri Strong and Mrs. Vahibe Strong had a baby son, Remzi Bogardus, on November 10, 1948 (A-Day). It weighed 7 pounds, 11 ounces, is 20½ inches, has red hair and blue eyes.

DEPARTMENT OF PATHOLOGY

Dr. and Mrs. Goldenberg had twin sons, Thomas Edward and John David, on October 11, 1948. Thomas Edward weighed 5 pounds 14 ounces, while John David weighed 6 pounds 14 ounces.

Book Review

THE SCIENTIFIC PAPER. By Sam F. Trelease, Columbia University. Cloth. Pp. 152, with 8 figures. The Williams & Wilkins Company, Baltimore 2, Maryland. 1947.

Reviewed by Jerome Litt

To those select few in the field of medicine who would eschew the actual practice of medicine to try their hand in the field of medical research — and to these few who would wish to convey their results in some fashion to their colleagues in the outside world — this small book will prove extremely beneficial for such matters.

The student who is confronted with the arduous task of "writing up" his data will find in this book many suggestions that should not only lighten his work, but enable him to present his material in a more effective way. It should be noted that one of the most important stages in any scientific investigation is the preparation of the results for publication, and that every student who is preparing for work in a scientific research field should realize early that proficiency in writing — like proficiency in laboratory manipulations — is a highly important part of his education.

While the directions given in this manual are, in the main, for the preparation of a thesis or dissertation, they apply also to the writing of other types of papers in science, agriculture, engineering, and medicine, and to the preparing of manuscripts of a more popular nature on scientfic subjects. The contents include such basic material as the use of tenses, punctuation, italics, numbers, capitals, etc., and valuable information is given concerning the logical presentation of ideas, and "making the paper interesting."

In short, this book is as indispensible to the aspirant of research as the thorough, concise, and chronological history of a patient's illness is to the thorough-going clinician.

Spectrophotometric Determination—

(Continued from page 13)

ish-violet color brought about by a reaction between the epinephrine and ferric ammonium oxalate.

2. The bluish-violet color which forms in the dialysate of minced adrenal glands has been found to have been formed by a reaction between an epinephrine-like substance and iron products from the food chopper.

BIBLIOGRAPHY

1. Folin, O., Cannon, W. B. and Denis, W., *J. Biol. Chem.*, 13, 477, 1912.

2. Edlbacher, S. and Leuthardt, Klin. Woshschr. 12, 1843, 1933.

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Editorials . . .

THE STORY OF A SUCCESSFUL ENDEAVOR

The Chicago Medical School was organized in 1912 as the Chicago Hospital College of Medicine and Surgery, chartered by the State of Illinois as a non-profit institution. In 1919 it was reorganized as The Chicago Medical School, at that time absorbing the Jenner Medical School. It was administered by a board of directors who served without compensation. Until 1925 the school had afternoon and evening sessions; from 1925 to 1927 the junior and senior classes attended day sessions only, and since 1927 there have been only day classes. The school acquired its present location in the west side medical center of Chicago in 1930.

Dr. John J. Sheinin, who has been inseparably connected with the history of the school, was appointed Professor and Chairman of the Department of Anatomy in 1932. He is responsible for the reorganization of the school and the improvement of its facilities since that time. In 1933 Dr. Sheinin built the library which is now a member of the Medical Library Association and the American Library Association. Also in that year Dr. Sheinin rebuilt the Anatomy Department, re-equipped the Dispensary, and in 1934 and 1935 he redesigned and equipped the amphitheaters and photographic departments. In November 1935 the Board of Trustees appointed Dr. John J. Sheinin Dean of The Chicago Medical School.

During the succeeding years the school was inspected several times by the Council on Medical Education of the American Medical Association and by the Association of American Medical Colleges, and each time Dr. Sheinin was praised for the advancements and improvements which he had instituted. In 1946 Mr. Lester N. Selig was elected Chairman of the Board of Trustees. The following year the inspecting committee of the Council on Medical Education of the American Medical Association evaluated the school as being of approved calibre for the pre-clinical years. In the summer of 1947 the

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Mount Sinai Hospital affiliated with the school and was converted into a university teaching hospital.

On November 9, 1948 the following announcement was made:

"The Chicago Medical School now offers an endcational program that meets the standards for an approved medical school. A joint decision to this effect was taken by the American Association of Medical Colleges and the Council on Education and Hospitals of the American Medical Association on November 9th as a result of the most survey of the school by representatives of these two organizations, conducted in October.

"Therefore, the school is now included on the list of approved medical colleges and hospitals of the A.M.A. and is admitted to membership in the A.A.M.C. The school is to be congratulated upon the progress it has made in the last year. Its Board of Trustees, consisting of citizens of vision and understanding, will be wise to realize that their work, effective as it has been, has only begun. Their efforts deserve widespread support."

With the realization of a goal which was achieved after twenty-two years of endeavor, the focus was placed on one man — a man to whom this momentous occasion was in a way a great personal victory — Dean John J. Sheinin.

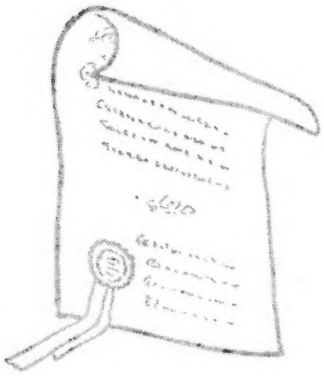
In recognition of Dr. Sheinin's herculean efforts many testimonials were organized by the students, the faculty, alumni, and friends. The first of these was a dinner tendered by the faculty and student body of The Chicago Medical School, which was held in December in the Grand Ballroom of the Palmer House. Mr. Lester N. Selig was chairman of the evening and introduced the speakers who expressed their appreciation to Dr. Sheinin. Then Professor Leslie B. Arey introduced the guest of honor with whom he has been associated for many years as teacher, colleague and friend. Dr. Sheinin conveyed to all present that a new era has begun for The Chicago Medical School, but that it is one in which there is still much to be accomplished. At this time the faculty and students announced that an artist had been commissioned to do a portrait of Dr. Sheinin, which will be placed in the library.

A week later the thirty Chicago Medical School Alumni on the staff of the South Chicago Community Hospital held a dinner in honor of Dean Sheinin to which all members of the staff of the hospital were invited. Dr. Sheinin spoke briefly, following which all present retired to watch professional entertainment.

The New York Alumni Chapter wishing to express their appreciation, organized a testimonial to honor Dean Sheinin which was held on December 26, 1948 at the Starlight Roof of the Waldorf Astoria Hotel in New York. Dr. Frederick Spector was the chairman, and Mr. Mark Sugarman introduced Dr. Sheinin to the 300 people present. Among the guests were Commissioner A. Stark, Commissioner of Commerce of the City of New York; Dr. Abraham Koplowitz, Past President of the Kings County Medical Society; and Dr. Jacob L. Lochner, Jr., the Secretary of the New York State Board of Examiners.

On February 19th the Chicago Chapter of the Alumni Association of The Chicago Medical School will further express their gratitude to Dr. Sheinin in the Gold Coast Room of the Drake Hotel here in Chicago.

It is very appropriate that these many groups honor Dean John J. Sheinin for his magnificent work, but a final and more lasting tribute will come to him from his students as they become the kind of physicians worthy of his life-long efforts on their behalf.



PRESENTED BY THE FACULTY OF
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ON DECEMBER 10, 1948

TO ALL TO WHOM THESE PRESENTS COME LET IT BE KNOWN THAT

Dr. John J. Sheinin

HAS RENDERED YEOMAN SERVICE IN THE INTEREST OF

The Chicago Medical School

Whereas, in the face of great odds and difficulties he successfully directed efforts which resulted in the development and recognition of a medical school of high standards; and

Whereas, he has made remarkable contributions toward the advancement of medical education; and

Whereas, he contributed immeasurably to the well-being of all associated with The Chicago Medical School; and

Whereas, he is a man of rare integrity and an intrepid champion of democracy, especially as it applies to medical education.
Be it therefore resolved:

That we, the Faculty of The Chicago Medical School, express our deep appreciation and regard, and do so indicate with our affixed signatures, this tenth day of December, nineteen hundred and forty-eight.

John J. Sheinin, Dean

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JOHN J. SHEININ, DEAN

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The entire student body turned out to welcome Dr. Sheinin on Nov. 11, 1948 (Photo by Scanlon)

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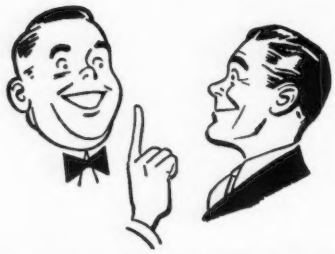

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On behalf of all students, Bernard Kleppel, President of the Senior Class, thanked Dr. Sheinin for his achievement. (Photo by Scanlon)

Later that morning, at a reception in the Library, Dr. Sheinin read the official statement of Approval to the assembled Faculty, students and guests. (Photo by Scanlon)

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(Continued from page 11)

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Bell, E. T. Experimental diabetes mellitus. c1948. 13D B 41

Blau, A. The master hand. 1946. 19 L B 61

Contributions to embryology, vol. 32 (No. 207-12) 1948. 3 G C 76

Eckstein, G. Everyday miracle. 1948. 1 Hb Ec 5

Hassin, G. B. Histopathology of the peripheral and C.N.S. 3d ed. 1948. 19 B H 27

Johnstone, R. T. Occupational medicine and industrial hygiene. 1948. 32L J 65

Magoun & Rhines. Spasticity. c. 1947. 19 J M 27

Methods in medical research, ed. by V. R. Potter, vol. 1. c. 1948. 7 As M 56

New York (state) Legislative Committee. Problem of cerebral palsy. 1948. 19 E N 48

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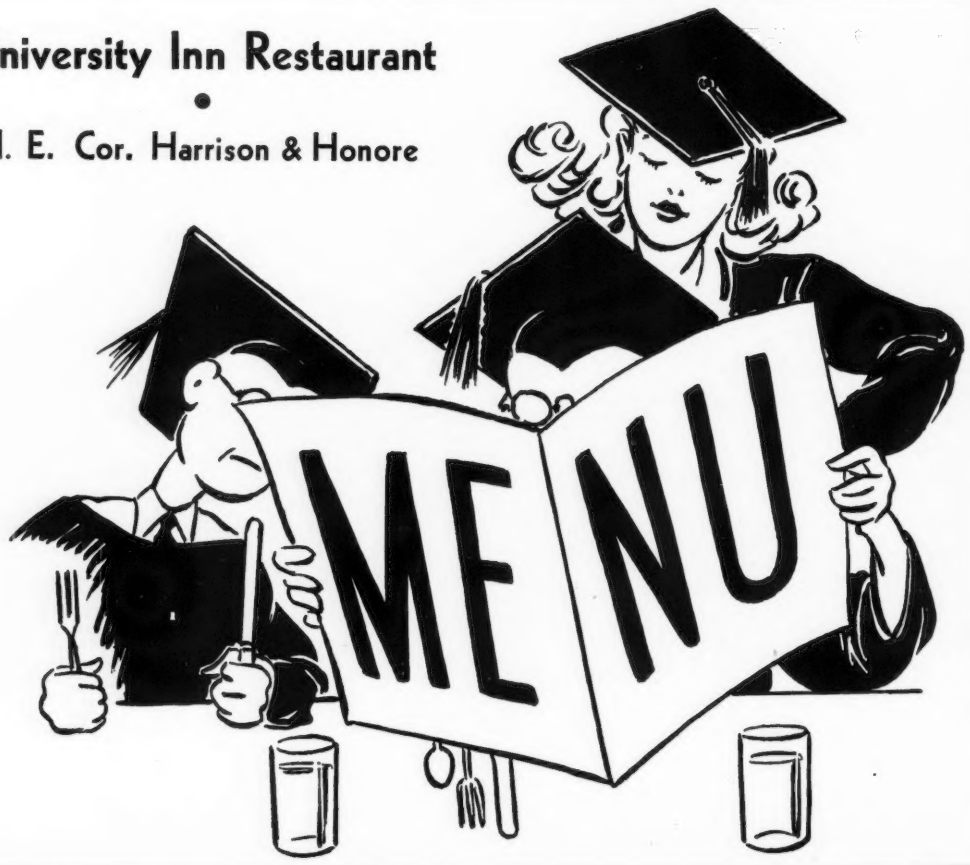

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SEMINARS—

(Continued from page 26)

stein, Asociate Prof. of Surgery, Northwestern University; Prof. of Surgery, Cook County Graduate School of Medicine; Attending Surgeon, Cook County Hospital, Chicago, Illinois.

May 11—To be announced.

May 18—"The Practical Approach to the Diagnosis and Management of Sterility." Dr. M. J. Nechtow, Associate in Obstetrics, Chicago Medical School, Chicago, Illinois.

May 23—"Determination of the Anesthetic of Choice." Dr. Ruth Weyl, Assistant Prof. of Anesthesiology, Chicago Medical School, Chicago, Illinois.

June 1—"Injuries of the Kidney." Dr. H. C. Rolnick, Prof. of Genito Urinary Surgery and Chairman of the Department of Urology, Chicago Medical School, Chicago, Illinois.

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